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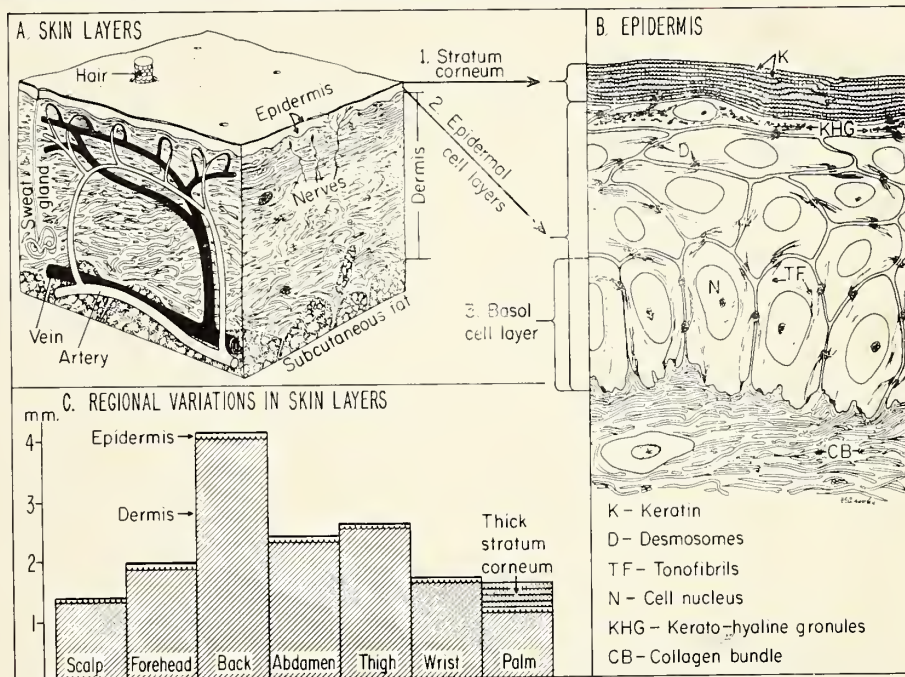


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DERMATOLOGY ISSUE: Sidney N. Klaus, M.D., Guest Editor



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The Skin: The Most Accessible Tissue of the Body Serves as a Potential Focus for Multidisciplinary Research

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The Skin A Potential Focus for Multidisciplinary Research

The skin of organisms living in a watery environment doesn't have to protect the animal against rapid fluctuations in temperature, humidity, concentration gradients, acceleration, toxic chemicals, radiation etc. The human skin does have the properties of protecting the delicate cells underneath against an unfriendly environment, so that the body remains remarkably undisturbed during wide fluctuations in environmental conditions. It is this tolerance of humans to environmental changes that has evoked interest among anatomists, physiologists, dermatologists and others to employ technics of physics, chemistry, various fields of engineering and many others to study the skin intensively as to how it accomplishes these complex functions.

Human skin is remarkably effective in retarding diffusion of gases, water and many types of chemicals. Most irritants and cellular poisons are unable to penetrate the skin with some exceptions such as mustard gas and ivy poisoning. Water will sometimes move through the skin as for example when humidity is 90 per cent mostly where the skin is thickest as at the soles of the feet. If the outside air is lower than 90 per cent humidity, then water will move out of the skin (insensible perspiration). Then there is a central point at which water neither enters or leaves, a point which is lowered in edema, menstruation or infectious illness. Pure water alone goes through the stratum corneum (see front cover) which is totally impermeable to salt. As one would expect from the wide variability in

skin morphology, the skin function as a diffusion barrier varies from primitive areas like the scrotum which readily transfers water and chemicals, to other areas not so permeable.

The skin also acts as an electrical and thermal barrier. Its electrical impedance is high and this explains the difficulty in capturing the surface potentials generated by the heart and brain. Its thermal barrier makes it possible to maintain a constant internal temperature in any climate, especially since most enzymes are sensitive to temperature change so that a drop of only a few degrees may inhibit their activity completely.

The skin is able to conserve or eliminate heat because it is equipped with networks of blood vessels in the dermis with capillary loops extending nearly to the surface. With these blood vessels wide open the skin is a most effective heat exchanger. The quantity of heat dissipated or conserved can be precisely regulated by controlling the blood content and blood flow through these vessels. There are sites at the base of the brain in animals which when warmed cause heat dissipation and when cooled, heat conservation. Investigation of biological temperature control is now becoming highly complex since it is of interest in terms of thermodynamics, control system analysis and environmental engineering.

It is now possible to visualize distribution of temperature gradients in the skin. Certain cholesterol esters remain colorless above and below 28-31°C. but colorful at these temperatures. In this way it has been found that temperature gradients

ABOUT THE COVER

"The cover in this issue of *Connecticut Medicine* is a schematic illustration of the important anatomic features of the skin. This illustration appeared in the October 21 issue of *Science Magazine* in an article entitled, *The Skin: The Most Accessible Tissue of the Body Serves as a Potential Focus for Multidisciplinary Research*. The authors teach at the University of Washington where Dr. Robert F. Rushmer is a Professor of Physiology and Biophysics and director of the Instrument Development Program; Dr. Konrad J. K. Buettner is a Professor of Atmospheric Sciences; Dr. George F. Odland is an Associate Professor of Medicine, Head of the Division of Dermatology, and Associate Professor of Biological Structure; and Dr. John M. Short is an Instructor in the Division of Dermatology. The illustration was prepared by the Department of Health Sciences Illustration, Mr. Thomas Stebbins, Director, by Miss Virginia Brooks."

vary from point to point and from moment to moment on the back of the hand or over superficial veins. Cool regions are found over the knuckles and over the nose and cheek. The phenomena so uncovered are complex because of variations in the property of the skin and in the environmental thermal load as well as with continual physical adjustments in sweating rate, skin blood flow and metabolic rate. A student of Rushmer, Douglas Housman, has derived a mathematical model for investigating the effects of environmental heat on the cutaneous thermal gradients.

The skin is also a barrier to radiation, protecting the underlying cells in varying degree from electromagnetic radiation such as soft X-ray, ultraviolet light, visible light and infrared wavelengths. Frequent application of ultraviolet light may cause loss of elasticity of skin, early aging and possibly even cancer. Excessive exposure to sunlight leads to the elaboration of melanin, the skin pigment responsible for suntan. The visible light penetrates deeper than the ultraviolet. However, our knowledge of the optical properties of skin is incomplete, since these properties vary with skin thickness and degree of pigmentation.

Vital information about the immediate environment is conveyed to the central nervous system from exquisitely sensitive nerve endings responding to touch, warming, cooling and pain. The sensitivity of these transducers is really remarkable. The Paccinian corpuscle is excited by mechanical deformation of .5 microns applied for 0.1 sec. Temperature sensations are elicited by two types of receptors; one responds to an increase in skin temperature by as little as .0015 calories/sq.cm./sec. Another responds to a temperature decrease of 0.004°C per sec. It is obvious that transducer principles and communication theory will need to be applied more fully to these energy converting nerve endings. Engineers can learn much on how to develop transducers of such size and sensitivity.

The skin serves as a flexible container for the body. Think of what forces are applied to it when one uses a screw driver to loosen a balky bolt. What strength there must be in the attachment between layers of cells in the skin and in the collagen fibers fastening the epidermis to underlying structures! These mechanical properties of skin are of vital importance to surgeons particularly in selecting sites for incisions or closing large defects. Kennedy et al² have begun reporting results of quantitative analysis of skin properties with particular concern for the problems of plastic surgery.

The dermis is of interest with reference to its tensile strength, heat exchange, energy conversion in sensory nerve endings, coding of information on nerve trunks, active transplant in glands, elastic and viscous moduli, stress strain relations, control of blood flow and blood content in superficial vessels. Temperature regulation is a fine example of a complex biological compensatory mechanism subject to control-system analysis. Data acquisition and analytical technics of engineers, physicists, chemists and mathematicians could contribute much to our understanding of skin function. The information would be of inestimable value to anatomists, physiologists and surgeons but most of all to dermatologists.

Comprehensive and quantitative descriptions of the skin would certainly provide a whole new range of knowledge and technology applicable to both normal and diseased skin. Up to the present diseases and lesions of the skin are generally identified primarily on the basis of their appearance. But we are entering a new era in which comprehensive description of the biological, physical and chemical properties of the skin will be forthcoming and with it will come clarification of the function of the skin in health and criteria for determining the presence of disease.

L.H.N.

References

1. Rushmer, R. F., Buettner, K. J. K., Short, J. M., Ochland, G. E. *Skin. Science*, 154, 33, Oct. 21, 1966.
2. Gibson, T., Kennedy, R. M. *Surg. Forum*, 14, 478. 1963.

Bacteria And The Skin

A question that has recently been raised by Lacey¹ is whether the long term effects of applying fat solvents including alcohol to an area of the skin may not be detrimental. He started his investigations with the premise that fatty acids derived from the skin lipids play an important part in controlling intravenous bacterial contamination. He showed that more staphylococci can be recovered from skin in which a culture has been allowed to dry if the area is pretreated with solvents including alcohol. His conclusion seemed warranted that the most likely explanation was that the solvent did elute from the skin natural antibacterial lipids. Lacey's observations do have relevance to the long established belief that bacteria multiply in the deep structure of the skin are then brought to the surface where the skin has highly efficient means for disposing any of the unwelcome bacteria.



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These beliefs have had much influence on views about the establishment of organisms on the skin and their removal from the hands of the surgeon, and the operative site of the patients skin.

How does the skin protect itself? This is a question that has a long history of contradictory studies and needs re-examination. Some workers are reported to believe that auto-disinfection occurs because fatty acids derived from the skin lipids were highly bactericidal. This, it appeared, was true only for streptococci and there was found to be much less activity against staphylococci. Ricketts et al actually concluded that the disappearance of *Escherichia* or *pseudomonas* from the skin was almost entirely by desiccation. In fact some claim that desiccation is the key factor and no other mechanism needs be postulated to account for the disappearance of bacteria from the skin.²

There is also room for more than one mechanism and the conflicting results might arise because any single observer uses different subjects, different methods, different bacterial species and probably different strains of the same organism. Then there is the question whether there is not also considerable variation from one part of the body to another. Also little attention has been given to the idea that perhaps skin lipids prevent too ready dispersal of the crumbling superficial layers of the epidermis. In fact substantial evidence exists that the natural habitat of bacteria is not the deeper structure of the skin (excepting of course the sebaceous follicles) but the three or four outer keratinized layers of the epidermis. Dispersal of the particles of the skin certainly makes a big contribution to the bacteria recovered from the air³ and visual proof has been presented that these airborne organisms are carried on epithelial fragments. The conclusion seems inescapable that if the cohesion of the upper layers of the skin is impaired then more skin particles and their associated organisms will be detached.

An unexpected finding is that the number of skin organisms liberated into the air is increased immediately after bathing.³ If we assume that soap removes skin lipids then it is easier to understand why after a bath there is more ready dispersal of superficial epithelial fragments. Another interesting observation is that of Blank and Coolidge⁴ which suggests that electrostatic charge may be an important part securing bacteria to keratin. Treatment of the skin with strong alkali such as soap may affect the skin charge and so facilitate the liberation of bacteria.

Those who set nurses or students the experiment of sampling the fingers before and after washing will be familiar with the finding that some of them always record increased bacterial counts.⁵ Such rapid increases in the number of recovered bacteria are much more likely to be due to physical effects rather than to impairments of antibacterial mechanisms. Similar phenomena may well play an important part in increasing the recovery of bacteria which have been applied to skin treated with potent lipid solvents.⁶

As a means of reducing the number of recoverable organisms from the skin efficacy of alcohol is in doubt. Whether the later results of interference with skin lipids are detrimental, will be established only by a thorough re-examination of the interaction of skin lipid and organism and their relative rates of accumulation. However, Bernard et al⁷ have recently demonstrated that the application of alcohol to the skin actually abolishes the increased output of skin bacteria and does not facilitate their liberation such as normally follows a shower-bath.

This story reveals that too much about the bacteria of the skin has been taken for granted and that previously supposed facts are poorly documented and some cherished beliefs are hard to substantiate and that much further work needs to be done on bacteria in the skin and how the skin protects the body against invasion of microorganisms.

L.H.N.

References

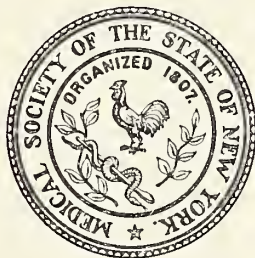
1. Lacey, R. W.: *Brit. Jr. Exp. Path.*, 49: 208, 1968.
2. *Lancet: Bacteria and the skin.* II October 19, 1968, p. 860.
3. Riley, R. L. and O'Grady, F.: *Airborne infection: transmission and control.* New York, 1961, p. 27.
4. Blank, I. H. and Coolidge, M. H.: *J. Invest. Derm.*, 1950, 11, 49.
5. Pillsbury, D. M. and Klegman, A. M. in *Modern trends in dermatology.* Edited by R. M. B. MacKenna, p. 187, London, 1954.
6. Lowbury, E. J. L. in *Skin bacteria and their role in infection.* Edited by H. I. Maibach and G. Hildick-Smith, p. 263, London, 1965.
7. Bernard, H. R., Speers, R., O'Grady, F. W. and Shooter, R. A.: *Arch. Surgery*, 11: 530, 1965.

Science Tools: 27: Radiologic Estimation Of Skin Thickness In Health And Disease

Measurements of the combined thickness of skin and subcutaneous fat by means of skin calipers is sometimes used in studies concerned with nutrition and obesity. However, measurements of the

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thickness of the skin alone has rarely been attempted. There is, however, little doubt that there is alteration in skin thickness in disease. It appears thick in acromegaly and myxedema. It appears thin in hyperthyroidism and hyperadrenalism. But evaluation of these changes by palpation alone is too inexact because confusion can arise from skin changes quite unrelated to its thickness. For example alterations in elastic fibers, differences in the amount of subcutaneous fat, variations in hydration found in edema and dehydration do introduce an element of uncertainty.

Animal studies of the corium layer have revealed a high collagen content which is one of the major sources of reserve protein in the body. If we could have precise measurements of this layer, perhaps we would be in possession of a useful index of the state of protein metabolism. This could be combined with the quantitative determination of hydroxyproline in the urine.

It is now possible to measure exactly skin thickness by a roentgen method. An oblong cedar block is applied firmly to the skin of the lateral aspect of the forearm at its point of greatest prominence. The central roentgen beam is then directed accurately in line with the flattened vertical surface of the skin. The resulting picture shows the skin as a lighter zone of decreased photographic density lying between darker zone produced by the overlying cedar block and the underlying subcutaneous tissue. Measurements are then made by a scaled magnifier to an accuracy of 0.1 mm. and then averaged along a length of 1 cm. Apparently alterations in block pressure did not affect measurements.

The study attempted to establish a precise normal range on skin thickness in normal adults both fifty-three men and one hundred and seventy-eight women and systematically determine the skin thickness in certain common endocrine and metabolic disorders. In the female the average thickness was 1.34 mm. regardless of age. In the males the mean skin thickness was 1.43.

The skin of the acromegalic patient is characteristically coarse, thick and leathery. In 9 women the range was from 1.65 to 2.40 mm. In twelve males mean skin thickness was 2.23. The differences values are quite striking. The thickness seems to appear early in the disease and one of the thickest measurements recorded was in a patient with acromegaly of apparent recent onset.

The converse was found in Cushing's disease due to either adenoma or bilateral adrenal hyperplasia.

In eight females the skin thickness averaged .91 mm. and when the patients were cured surgically the skin thickness returned to normal over a period of three to six months. In eleven patients who were receiving adrenal steroids for diseases such as rheumatoid arthritis, purpura, asthma, a trend towards thinning of the skin was revealed with an average thickness of 0.86 mm. The degree of change seemed to correlate well with duration and extent of therapy. One patient with sarcoidosis who had a skin thickness of 1.3 mm. before steroid therapy ended up with 1 mm. eighteen months later.

Apparently thyroid function had no effect on skin thickness. The values remained normal in eighteen hyperthyroid and eleven myxedematous females. The skin thickness was not altered in diabetes nor in obesity. However, in undernutrition from whatever source the skin thickness declined to below normal. What happens in various skin disorders needs urgent study. It appears that skin thickness increases in psoriasis and exfoliative dermatitis.

It would appear from Sheppard and Meema's¹ studies that skin thickness mirrors the state of body protein and structural collagen. This is perhaps why when in undernutrition the body protein pool is depleted, then skin thickness declines. The same explanation might be offered for the thinness of the skin in hyperadrenalism in which the thinness of the skin reflects protein loss and negative nitrogen balance. The anti-anabolic and catabolic properties of corticosteroids are well recognized. We know these agents inhibit production of collagen fibroblasts which results in poor tissue repairs. The obese patient, however, even when he loses weight loses fat not protein and consequently skin measurements do not show thickness changes.

It has been assumed that hyperthyroidism increased protein metabolic changes and that myxedema decreased protein metabolism from the normal. It was inferred from this assumption that hyperthyroidism increases collagen destruction and that increases in collagen formation occurs in myxedema. But neither hypo-nor hyperthyroidism affects skin thickness. Apparently we must accept the conclusion that in either case the protein balance is not altered whether there is increased destruction and production of protein or decreased production and destruction of protein.

The technique of measuring skin thickness must be extended to dermatologic disorders. For the present it seems valuable in screening out patients with true Cushing's from the obese and mildly

hypertensive diabetic with normal adrenocortical function. The technique can also help to differentiate acromegaly in whom neither the roentgenogram or sella turcica enlargement can be considered diagnostically significant.

L.H.N.

References

1. Sheppard R. H. and Meema, H. E.: Skin thickness in endocrine disease. *Ann. Int. Med.*, 66: 531, March 1967.
2. Lee, M. M. C.: Postmortem studies of skinfold caliper measurements and actual thickness of skin and subcutaneous tissue. *Hum. Biol.*, 37: 91, 1965.
3. Allison, J. B. and Wannemacher, R. W. J.: The concept and significance of labile and overall protein reserves of the body. *Amer. J. Clin. Nutr.*, 16: 445, 1965.
4. Steinbach, H. L., Feldman, R. and Goldberg, M. B.: Acromegaly. *Radiology*, 72: 535, 1959.

Unfavorable Consequences Of Pesticide Use

While yields may be increased with greater margins of profit by chemical spraying we must also recognize in what way these chemicals may adversely affect a whole spectrum of non-target organisms, not only when the poison is applied but as far as thousands of miles away from the site of application. To the ecologist concerned with the total environment these persistent pesticides pose many serious threats to our natural ecosystems. Every spray operation kills target and non-target organisms and the non target organisms may be the predators on the very organisms one is attempting to control and these losses extend far beyond the beneficial insects. For example in Florida in an attempt to kill sand flies, over a million fishes were killed with dieldrin and crustaceans were virtually exterminated.

In New Hampshire in 1963 an attempt was made to save elms from the dutch-elm beetle by spraying with DDT. Not only was the operation unsuccessful because not enough was known about the source of elm bark beetle, but 90 per cent of the robin population was destroyed. Another classic example of wide spread destruction on non-target organisms was the fiasco involving the fire ant eradication program in the southern states. In 1957 dieldrin and heptachlor were annually spread over two and one-half million acres. Wide destruction of vertebrate population resulted. There was damage to crops, wildlife, fish. Only later was it learned that the ant was not an economic pest but a nuisance. Had only a small percentage of the 2.4 million dollars wasted on indiscriminate sprays been directed toward basic research we might today be far ahead in the control of the fire ant.

One serious hazard of pesticides is their accumulation in the food chain. The persistence of the poison leads to its carriage from one organism to another in the food chain. As this occurs there is a gradual increase in the biocide at each higher trophic level. One example is the repeated spraying for pesty gnats in Clear Lake, California. The plankton collected 250 times more chemical than originally applied, the frogs 2,000 times more, the sunfish 12,000 times and the grebes 80,000 times and this led to total destruction of these birds that nested on the lake. The edible fish now caught reaches 7.7 ppm. above the maximum tolerance level set by the F.D.A.

Coming closer to home we find that Long Island tidal marshes have been sprayed against mosquitos for twenty years. The plankton show .04 ppm., shrimp .16 ppm., minnows 1-2 ppm., gulls 75.5 ppm. In general the DDT concentration in carnivorous birds were 10-100 times those in the fish they fed upon. Birds near the top of the food chain have DDT residues about a million times greater than the concentration in the water. Pesticide levels are now so high that certain populations are being subtly eliminated by food chain accumulations reaching toxic levels. At these levels the reproductive potential declines sharply. Many birds are now in serious trouble such as the bald eagle, osprey, hawks, herring gull and pheasants.¹

The synergistic effect of the pesticides is a grave consequence of their use. The interaction of two compounds may result in a third which is much more toxic than either one alone. For example nialthion is relatively "safe" because it is detoxified in the liver. However, if some other compound such as certain organic phosphates should destroy these enzymes then the toxicity of the new combination may be devastating. These subtle synergistic effects have opened a whole new field of investigation with many challenging problems. Doubtless we will find similarities in our multiple use of drugs in therapeutics.

Another serious problem arises from the chemicals migrating far away from the place of their original deposit. After two decades of intensive use pesticides are now distributed throughout the world far from any spraying. Penguins and crab-eating seals in the Antarctic are contaminated and fish far off the coasts of four continents now contain insecticides ranging from 1-300 ppm. in their fatty tissues.² The major rivers of our nation are contaminated by DDT. In 1963 the lower Mississippi experienced an extensive fish kill from DDT³

The chlorinated hydrocarbons are not readily broken down by biological agents such as bacteria and so year after year of spraying they accumulate progressively within a given ecosystem. On Long Island up to thirty-two pounds of DDT have been reported in the marsh mud due to accumulation of twenty years of spraying for mosquito control.⁴ When present in these quantities burrowing organisms and the detritus feeders can keep the residues in continuous circulation in the ecosystem. Many marine forms are extremely sensitive to minute amounts of insecticides. Fifty per cent of a shrimp population was killed with edrin 0.6 ppm. Even 1 ppm. will kill blue crabs within a week. Oysters have been reported to accumulate up to 70,000 ppm! Similar reports come from Green Bay in Lake Michigan⁵ where effluent enters from Door County which uses 70,000 pounds DDT annually! Accumulation of these biocides especially in food chains and their availability for recycling pose a most serious ecological problem.

Some effects of pesticides may be delayed for many years because of the persistent nature and tendency of certain insecticides to accumulate at toxic levels in the food chain. Man is often the consumer of food chain organisms accumulating pesticide residues. In the general population human tissues contain about 12 ppm. DDT derived materials. Those with meatless diets and the Eskimos store less. However, agricultural applicators and formulators of pesticide may store up to 600 ppm. DDT or 1,000 ppm. DDT derived components. Dieldrin and lindane are also stored in human tissues without occupational exposure.⁶ The possibility of synergistic effects involving DDT, dieldrin, lindane and other pollutants to which man is being exposed may result in unpredictable hazards. In fact it is now believed that pesticides may pose a genetic hazard.

At a recent conference of the New York Academy of Science, Dr. Onsy G. Fahmy warned that certain chlorinated hydrocarbons and organophosphates and carbamates were capable of disrupting the DNA molecule and that such mutations may not appear until as many as 40 generations later. This dismal picture grew worse with the statement of Dr. Verrett who pointed out that folpit and captan thought to be non toxic have chemical structure similar to thalidomide and might seriously jeopardize the integrity of human offspring.

We are obviously dealing with many unknowns in our widespread use of "safe" insecticides. We have no assurance that 12 ppm. DDT in our human

tissues, now above the permissible in marketable products for consumption may not be resulting in deleterious effects in future generations. Pesticides per se or synergisms resulting from their interaction could well plague man in now unforeseen unpredictable ways in the future. As Ruud warns "it would be somewhat more than embarrassing for our 'experts' to learn that significant effects do occur in the long term. One hundred and eight million human guinea pigs would have paid a high price for their trust."

Those who are seriously interested in promoting sound use of biocides must be fully cognizant of the counter forces in society who think in terms of whether it is good business to reduce the use of pesticides. They think of whether biological control of pests⁷ will make as much money, not of the health and the very future of the human race. The scientists who know the deleterious effects of biocides on our environment, and their challenge to mans very existence must somehow get this scientific knowledge translated into action through the sociopolitical pathways available to us. We must communicate a sound science to society and see that sound scientific knowledge is translated into reality. Our survival on this planet may well depend on how well we can make this translation before it is too late.

L.H.N.

References

1. Niering, W. A.: The effects of pesticides. *Bioscience*, 18: 869, Sept. 1968.
2. Anonymous 1966. Fish, wildlife and pesticides. U.S. Dept. of Interior Supt. of Doc. p. 12.
3. Breidenbach, A. W. et al: Chlorinated hydrocarbons pesticides in major basins 1957-1965. Public Health Dept., 82: 139.
4. Woodwill, G. M., Wurster, Jr., C. F. and Isaacson, P. A.: DDT residues in an east coast estuary: a case of biological concentration of a persistent insecticide. *Science*, 156: 821, 1967.
5. Hickey, J. J. and Keith, J. A.: Pesticides in Lake Michigan ecosystem, 1964 in *The effects of pesticides on fish and wildlife*. U.S. Dept. Interior Fish and Wildlife Service.
6. Durham, W. F.: Effects of pesticides on man 1965 in C. O. Chichester ed *Research in pesticides*. Academic Press, Inc., New York.
7. Nahum, L. H.: Pest control by Biologic agents. *Conn. Med.* 31: 826, December 1967.

Late Consequences Of Torture

It is now well documented what has always been suspected that survivors of torture show permanent and progressive effects of trauma to the head in the form of physical and also affective disorders. Among Jewish survivors of Hitlerite concentration

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camps in which torture and starvation were the rule, there appeared to be little evidence of organic brain disease, but extreme and prolonged anxiety combined with continued insecurity long after rescue. However, we do not know anything about those that were killed in the gas chambers among whom probably were those who also had organic brain damage as a consequence of physical brutality. British prisoners of war in the hands of the Japanese were much afflicted by disease and malnutrition, but not many were subjected to the kind of torture that the Norwegian underground fighters received at the hand of the Hitlerite interrogation.

Of the Norwegians imprisoned by German occupation forces during 1939-45, a substantial proportion made an apparently good recovery after liberation. A few years later, however, some began to suffer from disabilities which seriously interfered with working capacity and social adjustment. At first because of the lack of any very distinctive physical component these disabilities received less attention than they deserved. Pension difficulties followed and the Norwegian Association for the War Disabled promoted an investigation by the Department of Social Medicine and Neurology of the University of Oslo. This has clearly established that these prisoners have a major genuine and characteristic disability arising from organic and affective disorders of the brain.

Professor Axel Strøm and his collaborators spent six years on a very thorough investigation of 227 patients of whom 180 had wholly war-conditioned disability and 28 partly war-conditioned. They established that the group were a better than average sample of the population before their captivity, were in better mental health and social adjustment. Nearly all had suffered heavy and repeated trauma often including head injuries combined with severe and prolonged anxiety. Malnutrition and disease were also of course universal. Evidence of organic brain disease was sought by a very full neurological investigation including examination of the cerebrospinal fluid, electroencephalogram and pneumoencephalography.

Multiple indications of encephalopathy were found in 184 cases and single signs in another 23. Psychometric tests of intellectual deterioration correlated closely with the degree of brain damage. Affective disorders were also present in 202 chiefly emotional liability, dysphoria, depression, persistent anxiety, and sleeplessness. Nightmares were particularly common. The organic brain damage and the affective disorders were present in most of

the subjects. Nevertheless to some extent it seemed to Professor Strøm's group that in some they may have been independent, admittedly a particularly difficult differentiation. The extent of organic damage is closely related to the amount of physical trauma especially to the head. On the other hand the degree of affective disorders correlated well with the amount of anxiety suffered.

It is important that the existence of permanent and progressive effects of such trauma has been so well established perhaps the more so now that we are no longer as sure as we were that nothing like it can ever happen again. Who knows how many of the war prisoners in Vietnam are being subjected to physical torture and what the late consequences will be when the survivors are liberated. Who can estimate the late consequences of the innumerable cracked skulls that are occurring almost daily as our societal violence grows? Who can estimate the late consequences of head injuries sustained in traffic accidents?

The work of the Oslo team has alerted the medical profession to the late consequences not only of torture, but of trauma to the head whether from a billy club, automobile or other source. We from now on must take seriously any affective disorder following trauma especially to the head for we now know it can lead to permanent and progressive brain disease with both organic and affective symptoms.

L.H.N.

References

1. Late effects of torture. *Lancet*, II: 721, Sept. 28, 1968.
2. Norwegian concentration camp survivors. Edited by Axel Strøm, Professor of social medicine. University of Oslo—Oslo Universitets forlaget. New York Humanities Press, 1968. pp. 186. N. Kr 48.

The Role Of Vasoactive Chemicals In The Control Of Peripheral Blood Flow

Vasoactive chemicals have long been linked to metabolism of tissues causing local regulation of blood flow. First it was observed in skeletal muscle following contraction (active or exercise hyperemia). Since then this attractive hypothesis has been extended to other tissues and other types of regulation of blood flow. In the simplest form of the hypothesis it is proposed that changes in metabolism or blood flow are followed by alterations in the concentration of oxygen or vasodilator metabolites in the tissue fluid surrounding the arterioles. These

alterations then result in active vasomotion that adjusts flow to a level more appropriate to the rate of metabolism. Thus increase in metabolism from contraction of a muscle decreases the oxygen concentration or increases concentration of vasodilator metabolites in tissue fluid resulting in active arteriolar dilatation and this in turn increases blood flow to a level required by the new level of metabolism.

Similar changes would follow a decrease in flow caused by a fall in perfusion pressure. This fall could occur in shock or could result from arterial disease that reduces flow to the involved area. As a consequence vasodilation could result and gradual restoration of flow to an affected limb would result. It is this mechanism that is presumed to operate in opening collateral channels in arterial disease. And it is this mechanism that is employed by graded exercise to achieve better flow rates in affected organs. The reverse of course would follow a decrease in metabolism or an increase in flow. It is now fairly well established that by decreasing flow or increasing metabolism there results in almost the same degree active vasodilatation. And more recently it has also been demonstrated experimentally that many vascular beds respond to an increase in blood flow with active vasoconstriction.

Bio-assay studies clearly show that the concentration of vasoactive substances is altered in venous blood during local regulation of blood flow.² Many substances have been assigned to this role at one time or another as a result of the chemical analysis of venous blood and tissues. Among these are acetylcholine, histamin, serotonin, bradykinin.^{3, 4} What about oxygen, hydrogen, potassium, adenosine and adenine nucleotides. Haddy and Scott¹ present very good evidence that while oxygen will dilate vessels when its concentration falls well below that of venous blood, low oxygen is not a complete explanation for the regulation of blood flow as metabolism of an organ increases. Neither is hydrogen a good enough explanation because vasodilatation occurs long before the pH. falls to a level low enough to effect increased blood flow. Therefore other factors besides O₂ + hydrogen play a more important role in the vascular responses to changes in flow and metabolism.

Potassium could play a role in skeletal muscle, but in heart muscle it does not.⁵ This ion rises in venous blood of active muscles up to 0.8 to 0.95 meq./liter. The opposite also occurs. Local reduction in K. produces a rise in resistance to flow

through kidney, limb, and muscle. In heart muscle the same deficit increases myocardial contractility without raising resistance. Adenine and adenine nucleotides are firmly linked to regulation of the coronary circulation during alteration of blood flow and metabolism but we are still not sure about their effects on blood flow in other tissues. Lactate and pyruvate have also been found barely active in regulating local blood flow.

Other factors clearly participate in local regulation of blood flow perhaps the most important of these being active vasomotion subsequent to some direct effect of changes in transmural pressure on the smooth muscle cell in the wall of the arteriole the so called myogenic or Bayliss⁶ response. Thus it seems likely that two or more chemicals operate simultaneously and perhaps the dominant chemicals are not the same in all organs. Furthermore in a given organ the participating chemicals may differ when local regulation is elicited on the one hand by change in flow and on the other hand by change in metabolism.

There is one group of chemicals the group of polypeptides known as kinins that have very potent biological activities. They are capable of influencing smooth muscle contraction, inducing hypotension, increasing blood flow, and neurovascular permeability. They incite pain and perhaps cause the emigration of granulocytic leucocytes. The kinins can induce many changes resembling those seen in inflammation and this ability has supported the proposal that kinins have a primary etiologic role in the development of the acute inflammatory process.⁴ They have also been implicated in several physiologic processes including regulation of blood flow in the salivary gland, constriction of the ductus arteriosus after birth.

Kinins have also been implicated in the pathogenesis of various forms of inflammatory diseases, the Schwartzman phenomenon, shock, angioneurotic edema, migraine headache and acute inflammation associated with thermal burns. Thus there exists an interrelation of the nervous system, inflammatory response and kinin-like activity.

The possible role of kinins in disease are exciting. If the kinins do have a significant role and there is much evidence in support of this view, the next step is to try to identify the biochemical steps that induce the many alterations that characterize the disease process. In turn we may anticipate the development of more rational and improved therapies.

L.H.N.



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during therapy, the drug should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Severe salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients.

Adverse Reactions: The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. (B) 46-600-C

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References

1. Haddy, F. J. and Scott, J. B.: Metabolically linked vasoactive chemicals in local regulation of blood flow. *Physiol. Rev.*, 48: 688, Oct. 1968.
2. Altura, M. B. and Zweifach, B. W.: Pharmacologic properties of antihistamines in relation to vascular reactivity. *Am. J. Physiol.*, 209: 550, 1965.
3. Nahum, L. H.: Bradykinin: A vasodepressor polypeptide. *Conn. Med.*, 26: 124, February 1962.
4. Kellermeyer, R. W. and Graham, Jr., R. C.: Kinins possible physiologic and pathologic roles in man. *New Eng. J. Med.*, 279: 859, October 17, 1968.
5. Bacaner, M. B., Lioy, F. and Visscher, M. B.: Induced change in heart metabolism as a primary determinant of heart performance. *Am. J. Physiol.*, 209: 519, 1965.
6. Bayliss, W. M.: On the local reaction of the arterial wall to changes in internal pressure. *J. Physiol. (London)*, 28: 220, 1902.

The Computer And The Doctor: Servant And Master

When a patient enters a consulting room a clinician will perceive his color, his debility, age, sex, nervousness, respirations and much else without any information being formally exchanged. A computer in the place of the clinician would, like any other machine perceive nothing. This raises the basic question to what extent are we aware of our own intellectual processes when we grapple with the problem of diagnosis? To what extent are we aware of our reasoning processes of the alternative choices open to us in determining upon a plan of therapy? To what extent can we carry in our minds all the accumulated information required to understand the problems involved in diagnosing and treating any individual patient? What can the computer do in these areas?

There is now recognized the immense potential of computers in epidemiological research both in infections and chronic disease. There are ways in which computers will be able to do some of the work of the doctor. The day may be at hand when a doctor in a hospital ward or even in general practice will be dialing a number or perhaps using a typewriter keyboard and be able to have the case history of his patient projected on a special television screen. Through the processes of record linkage, information from several sources may be included. A similar system is already being used by the big airlines for tracing seat reservations.

With the help of modern automatic biochemical equipment such as the auto-analyzer computers can produce a printed statement of the biochemical content of a patient's blood within an hour of venipuncture and show how each result compares

with the normal range for the persons age and sex. Computers can now undertake the complicated task of planning the optimum distribution of dosage per patients who are to have cancer treated by radiotherapy. Improvement in telephone communication is making it possible for small departments to "consult" computers elsewhere. Indeed E. W. Emery of University College Hospital reports¹ that with the help of Telex he obtains a treatment plan from a computer in the U.S.A. within a few minutes.

Computers can also plot data, submit them to logarithmic or any other transformation and plot them again. They can prepare reading lists and even scan articles they have selected to give some idea of the content. Computers are being taught how to count chromosomes. In these and many other roles the computer is servant and man its master. For the computer to offer the best it must have the most skillful master. It takes but one great master to benefit a whole world through the computer that he has programmed.

The servant can also teach the master and nowhere is this more persistently emphasized than in the role of computer diagnosis. The computer is utterly uncompromising in its demand for clear instructions and this demand reaches far beyond the habitual skills associated with the art of diagnosis. Computers are forcing doctors to pay more attention to the precision with which they use words, the logic of their sentence construction and the rationale behind the preparation of case records.

It is quite likely that the computer will turn medicine from art to science and even mathematical science. Perhaps this sounds a bit "out" to the physician whose daily concern is the routine management of common illness but the prediction probably will turn out to be right. A glance at the fundamental studies by Professor Feinstein² at Yale on employing mathematical tools in diagnosis and prognosis will reveal that the prediction is near realization. The computer is already helping us enormously in our daily work but perhaps its greatest service may prove to be its ruthless requirement for us to know the logical foundation of medical diagnosis,³ to know the method of multiple working hypotheses in a final diagnosis (what some call "lateral reasoning"), to demand for us to understand the meaning of words and sentence structure and to be logical.

If we are to have a science of clinical medicine then the computer can help us, but first we need

a new vocabulary which can explicitly state the nature of the symptoms, more precise clinical observation, the varied elements in physical signs, so that they can be enumerated and analyzed in the same way as other data are analyzed that are obtained in a laboratory experiment. Fed into a computer, the servant will really serve and the master will really teach.

L.H.N.

References

1. Doctors and computers. *Brit. Med. J.*, 4: 137, 1968.
2. *Clinical Judgement*. A. R. Feinstein. Williams and Wilkins, Baltimore, 1967.
3. Nahum, L. H.: The computer in diagnosis and treatment. *Conn. Med.*, 29: 429, June 1965.

New Adventures In Brain Science

Brain research is the ultimate problem confronting man. In modern brain research we are grappling with the same problems man has been trying to understand about himself for ages but now we realize that to understand ourselves it is essential to understand our brains. In terms of its complexity the problem is so enormous that it is much bigger than the whole problem of cosmology. Obviously also it is a much more important problem to us. The extent to which we have a better understanding of our brain we will have a richer appreciation of ourselves, of our fellow men and also of society and in fact of the whole world and its problems.

Thus far the adventure in brain science has been restricted to neurobiologists, neuro anatomists and neurophysiologists. Actually it must be a cooperative enterprise of a wide range of scientific disciplines. Chemists communication engineers and molecular biologists have already moved in. For example¹ Dr. Samuel Bogoch, Professor of Biochemistry at Boston University reported at the American Psychiatric Association in Boston in May that he and his group found sixteen discrete groups of brain glycoproteins or mucoids to date three of them molecules engaged in memory and learning. In carrier pigeons trained by operant conditioning, two such molecular groups appear in the early stages of learning and one in the memory phase—necessary for a lasting memory trace. These glycoproteins are also present in mammals and man. One is present in human embryos as early as the 15th week of gestation when the gray matter begins to form. Where such findings might lead is speculative whether it be to practical ways to assist learning potential by biochemical or nutritional means,

or to retard senescent change or to provide a new treatment to approach mental illness.

Eventually all the disciplines including physics and mathematics will be contributing and perhaps in the next few decades most of the greatest scientists of the world will be working on the brain. This will be made possible by the fantastic technical developments which have occurred. In neurophysiology it has been possible to identify the behavior patterns of the various types of cells among the 30,000 million neurons that make up our brains. Eccles and his group² have studied a number of them in great detail. Their chemical life, their physiological life, their interaction with one another and the ways in which they transform information, has been studied by the microelectrode first introduced by Ralph Gerard in Chicago.

The microelectrode together with neurochemistry and electron microscopy promise a rapid progress in the area of neurogenesis, the problem of how the brain gets put together from the chemical instructions of DNA. These techniques combined with brain tissue culture whereby implanted parts of the nervous system can be studied should soon give us a detailed understanding of how chemical instructions cause fibers to grow from nerve cells and establish functionally significant connections with other nerve cells. Because of the electron-microscope, the anatomist can now look at the level of the really interesting parts of the living nerve cell and its organization. However, conventional anatomy still has the task of working out the pathways that connect the myriad subsystems of the brain.

Neurochemistry as noted above can provide the key to some of the most perplexing problems in brain science. Not only is the problem of how the brain is put together of immense interest but also the chemical specifically involved in its normal activities, the day to day metabolism, all the membrane phenomena, the pumping of ions and the sensing and recognition of cell surfaces all are coming in for study. How does a fiber grow to make a distant connection with the right nerve cell? Does it smell its way as it were detecting highly specific molecules? Neurochemists as they refine their techniques down to the level of nerve-cell operation should begin to furnish some answers.

The pattern of organization of the brain in which the units are joined together requires much attention. How does the incredibly detailed connectivity that is present at birth come about and how does it keep changing through life in the

learning process? The brain contains all kinds of extremely clean circuits and is the best bit of communication design imaginable. To understand this will require neural communication people with background in the computer and information science. Although they are relatively new in the field, there is a fantastic future ahead for them.

Finally there is the study of behavior. That is what the brain is for were told, to give appropriate behavior to the ever changing situations confronting the organism, subtle behavior, skillful behavior, intelligent behavior that incorporates memory of the past. Besides behavior of course are the experiences, the "inner" experiences as well as behavior that the brain performs. Eccles study of the behavior of the cerebellum are models of the future brain research. The cerebellum is a kind of computer that coordinates muscular movement of vertebrates. In its function it exhibits "learned" behavior. Because the cerebellum is one of the relatively simple subsystems of the brain there is a chance we may be able to solve within the next few years the problem of how it functions. We cannot overdo our scientific efforts in trying to understand the brain. The problem in its totality is worth more than all the other problems confronting science.

To pursue answers to many of the meaningful questions there will emerge a common enterprise among interdisciplinary groups whose members can work as a team. Eccles himself has written a book on the cerebellum with a neuroanatomist and a neurophysiologist. Soon neurocommunications people will be working with him with their theory and techniques. There are people now coming into the field of brain science with very good computer techniques and expert theoretical knowledge, but they will have to team up with people who have knowledge of the anatomical and physiological reality of the brain.

L.H.N.

References

1. Randal, J.: Biological psychiatry. *Bio Science*, 18: 709, July 1968.
2. Eccles, J.: Brain research—the ultimate problem confronting man. *Scientific Research*, 3: 30, September 30, 1968.

Orthomolecular Psychiatry: III. Treating Mongolism With 5-Hydroxy Tryptophan

An important experiment is being conducted at the Children's Hospital in Washington D.C. since early 1967 on treatment of mongolism with 5-hydroxy tryptophan. One child in every 600 born is

afflicted with this disorder. Of these the preponderance have an extra chromosome in the 21 position, the infants have cells with triploid instead of diploid chromosomes. The remaining mongoloids derive their handicap from chromosomal translocations. The mongolism occurs with about the same frequency in both sexes and in all socioeconomic and racial groups.

In the experiment, infants are started on oral therapy between the second and fourth day of life. Dosage needs to be carefully determined but once adequate is easy to maintain. If the child is not getting enough of the amino-acid his tongue begins to protrude. If too much 5-hydroxy tryptophan is being used there may be seizures and spastic arching of the back. One can easily distinguish between infants in the control group and experimental groups merely by observing the child's posture. Those children receiving the amino-acid are observably less placid and clearly more alert.

The rationale for the treatment is based upon the finding that children with slanting eyes and protruding tongues that are characteristic of Downs syndrome are born with normal or near normal levels of serotonin which then drops two to four days after birth and then remain permanently depressed. 5-hydroxy tryptophan is a precursor of serotonin and being a small molecule like glucose, can pass the blood brain barrier and become converted to serotonin in the brain. The thinking therefore was that by administering a serotonin precursor it should boost serotonin brain levels enough to compensate for the otherwise chemical deprivation that heredity has decreed.

The immediate response to 5-hydroxy-tryptophan is often dramatic. An infant who is limp and lethargic one day is active and able to hold its head up when properly supported the next day. Treated children have walked and talked far earlier than such youngsters ordinarily do and some have reached these developmental landmarks at the normal time. What is not yet known, however, is what effect if any the chemical may have on intellectual potential. Measurements of intelligence are not considered to be predictive of school success until a child is three years of age. The oldest child in the observational group, there are forty in all, will not be this age until 1969. Furthermore one would not expect real gain in intelligence unless head size began to approach normal limits. So far the treated children's heads have been no larger than those of untreated children. Thus perhaps there will have to be added another factor as yet

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Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics—has resulted in dependence or habituation. Withdraw gradually after prolonged excessive dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance, with resultant slowed reactions and impaired judgment and coordination. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, patients should not operate machinery or drive. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously and in small amounts to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with gastric lavage and appropriate symptomatic therapy (CNS stimulants and pressor amines as indicated). Two instances of accidental or intentional significant overdosage with ethoheptazine and aspirin have been reported. These were accompanied by CNS depression (drowsiness and lightheadedness) but resulted in uneventful recovery. On basis of pharmacologic data, CNS stimulation could be anticipated, with nausea, vomiting and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]).

Adverse Reactions: Ethoheptazine and aspirin may cause nausea with or without vomiting and epigastric distress, in a small percentage of patients. Dizziness is rare at recommended dosage. Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses. Such patients may have had no previous contact with meprobamate and may or may not have an allergic history. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, discontinue meprobamate; do not reinstitute. Severe reactions, observed very rarely, include fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. These cases should be treated symptomatically including, when indicated, such medication as epinephrine, antihistamine and possibly hydrocortisone. A few cases of leukopenia, usually transient, have been reported on continuous use. Rarely, aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported, almost always in presence of known toxic agents.

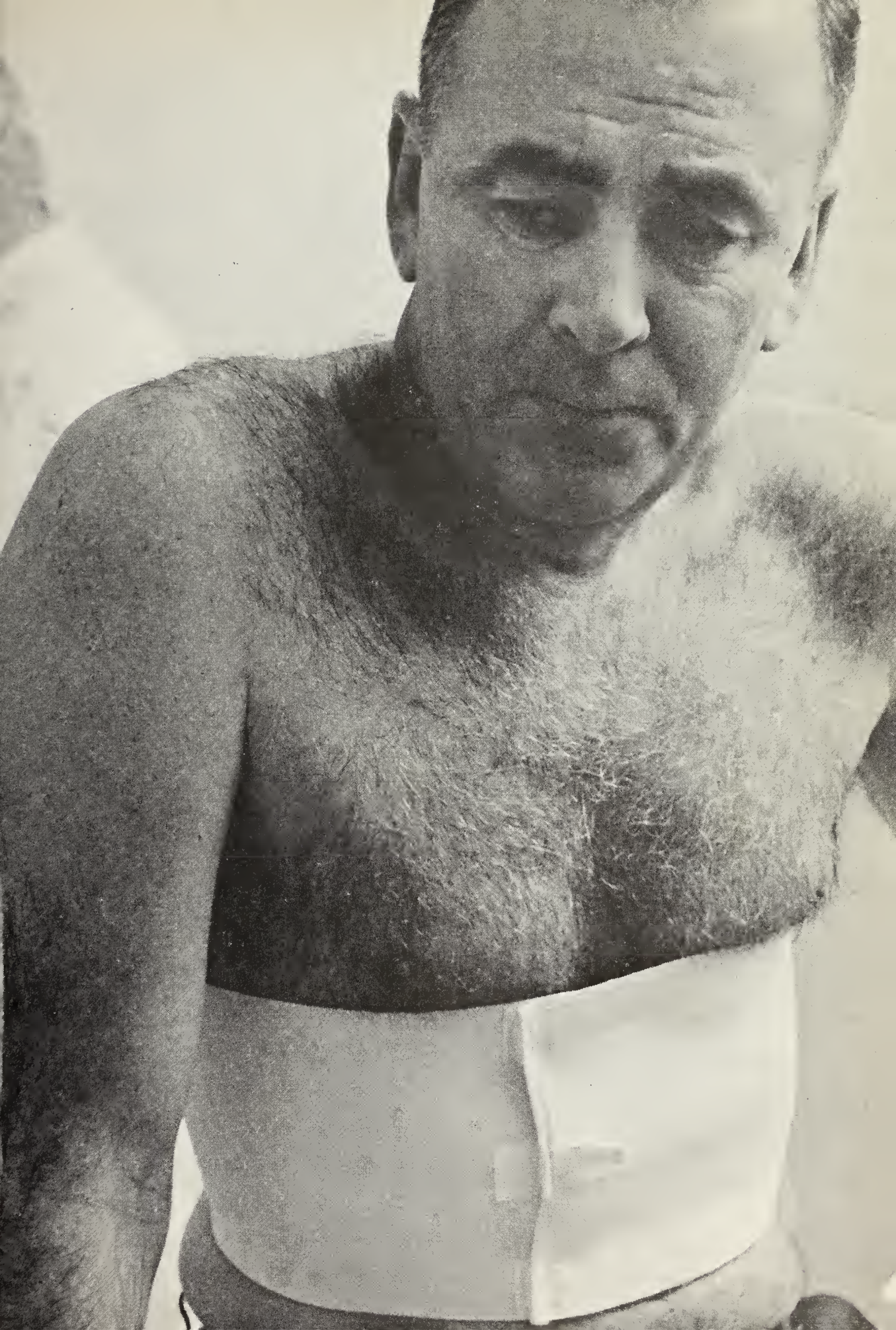
Overdosage: See precautions section for management of overdosage.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

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unknown, a nerve growth factor, that will promote growth of the brain during the critical first four years of life.

It may well turn out that unless the brain can be made to grow, that 5-hydroxy tryptophan will do far more for the child physically than it does intellectually. Dr. Mary Barzelon who is in charge of the experiment is not at all sure about whether intellectual growth will keep pace with improvement in physical vigor. Even so it may at least be a cost-saver, for ordinarily a child with Down's syndrome is unusually susceptible to infection and must frequently be hospitalized. The children maintained on 5-hydroxy tryptophan rarely suffer from infection perhaps because of their greater vigor and activity.

If the treatment is successful, then daily dosage with the amino-acid precursor of serotonin could probably be discontinued when the child is four to five years of age at which time brain size and therefore intellectual potential usually reaches its maximum. It will be important to assess whether treated children have attained normal or near normal intelligence but also what other factors may have played a role, since it is easy to distinguish between treated and untreated infants. One must be sure to recognize the role of parental and medical attitudes, since these may obscure the true role of the amino-acid precursor.

What is hoped for is an I.Q. of at least 60 generally considered by psychologists and educators to be the level a youngster needs to have to be trained. Unless the child with Down's is a mosaic i.e. a person whose cell population is partly diploid and partly triploid for the 21 chromosome for this group the I.Q. levels are ordinarily in a far lower range than 60.

The outcome of the 5-hydroxy tryptophan experiment is likely to have an impact not only on the treatment of mongolism but on the therapy of many chromosomal aberrations and inborn errors of metabolism that result in intellectual deficit most of which distort the role of serotonin in some undesirable way. Because investigators are increasingly interested in the biochemical mechanisms by which early protein calorie deprivations also takes its toll on the intellect, there may be a whole new field here for nutritionists as well as molecular psychiatrists.

L.H.N.

Reference

1. Randal, J.: Biological psychiatry. *Bio Science*, 18: 709, July 1968.

Research Related To Dentistry: III. Relation Between Oral And Biological Systems

The current research in oral biology has already demonstrated close relationships between many biological disciplines. For example nutritional deficiencies commonly affect oral tissues and are frequently manifested early in the mouth. In one study¹ for example 36 per cent of 914 patients hospitalized because of nutritional problems had pain of the oral soft tissues and a loss of tongue coating or both as the primary symptom. The lengths of the filiform papillae which comprise most of the covering of the tongue depend upon the constant and rapid proliferation of epithelial cells. An interruption of a systemic metabolic process affecting all replication may then be manifested clinically as a loss of tongue coating. Readily available biopsy specimens from the mouth should prove useful in diagnosis and assessment of treatment in a variety of abnormal systemic conditions.

Already applicable in an analogous fashion are studies in oral exfoliative cytology. Cells obtained from the surface of the oral epithelium could provide a ready source of material for chromosomal studies of all types. This approach was the basis for sex determination of the female athletes at the recent Olympic games in France. An evaluation of the nuclear dimensions of oral epithelial cells has provided an accurate measure of the systemic response to treatment of pernicious anemia.

Diabetes mellitus is a complex disease of great interest to the dentist. The clinical management of periodontal disease cannot be achieved in a patient with uncontrolled diabetes. It has also been shown that the average dosage of insulin required to control blood glucose levels in patients suffering from both diabetes and periodontal disease is significantly decreased following adequate periodontal therapy.

Periodontal tissues exhibit an exaggerated response to even minor sources of irritation during pregnancy. It is for this reason that gingivitis and benign overgrowth of the gingiva complicate the pregnancy of many women. Paradoxically women

with dermatologic conditions involving the mouth or with chronic ulcerative disease of the oral mucosa frequently experience a marked improvement in these conditions when they do become pregnant. Some drugs like dilantin also lead to an overgrowth of the connective tissue of the gingiva. It has been shown that a very substantial increase in collagenase activity of the involved connective tissue occurs and yet it is only this connective tissue of the body that responds to dilantin.

Thus far little attention has been directed towards absorption through the oral mucosa of agents taken by mouth. Such absorption does occur as any patient with angina knows when he places a nitroglycerin tablet under the tongue. To what extent is such absorption involved in the short and long range response to tobacco? Are agents altered in the process of absorption? We know that allergic responses will follow after topical application of a drug on oral tissues.

We know that within minutes following each tooth extraction or other surgical procedure in the mouth, oral bacteria can be isolated from peripheral blood. The bacteremia usually involves non-pathogenic bacteria and is transient. At present we think that this phenomenon is of no great significance except in patients with rheumatic or congenital heart disease, where however it might lead to bacterial endocarditis. Such a serious event should be borne in mind and prophylactic antibiotic therapy is now the accepted practice. There may be other less obvious but more complex implications of the bacteremia which is currently viewed as a routine event in daily practice such as a sequel of kidney disease.

Readily accessible tissues of the mouth offer an excellent opportunity for the oncologist to study precancerous lesions and malignant transformations. Dentists will at times see whitish raised hyperkeratinized areas of the mucosa and should remember that a large percentage of oral cancer develops in or from these patches. Approximately 5 per cent of all cancer does begin in the oral cavity. The vast majority of these malignancies are epidermoid carcinoma characterized by a lack of pain and a tendency toward early metastasis, probably as a result of rich vascularity of oral tissues and their high mobility. Much effort has been directed toward study of the development of oral cancer in the cheek pouch of the hamster where experi-

mental cancer can be induced chemically by means of well standardized and carefully controlled techniques.

Another important area in which dental researchers have directed their attention is in the techniques and immunology of tooth transplantation in anticipation of the day when tooth storage banks may be founded in many cities. Autogenous transplants, the transplantation of teeth within the same jaw, can now be accomplished with a high degree of success. Homologous and heterologous transplants however are rejected in most cases as a result of the immune reaction. Teeth seem to retain their antigenic properties even after being rendered non-vital by removal of the pulp and treatment with root canal filling materials.

If the components of saliva from healthy patients were fully known and the normal ranges of each component established, then saliva, like blood, could become a useful indicator of some aspects of systemic health. For example it is now known that guanethidine alters the chemistry of saliva from the submaxillary glands in animals and humans. This drug temporarily improves the chemical balance of organic compounds of submaxillary gland saliva in children with cystic fibrosis without changing the concentrations of calcium, sodium and potassium. This illustrates the need of dentists who inspect the mouth to be aware of drugs as they influence the saliva as well as the gingiva. This means that the dentist should explore the mouth of his patient and know something about his systemic condition and drugs the patient is taking.

It is clear enough from what has been said that the base of dental sciences is broadening and that the potential for success and accomplishment is directly related to amount of scientific manpower that is devoted to dental research and related fields. This means there must be unqualified acceptance of research as part of the responsibility of the dental academicians. Once scientists become aware of the implications of their work for dental research then appropriate depth will be added to the breadth that has already been achieved by the dental scientists in the last twenty years since NIDR was founded.

L.H.N.

Reference

1. Morris, A. L. and Greulich, R. C.: Dental research: the past two decades. *Science*, 160: 108, June 7, 1968.

Foreword

This is the first issue of *Connecticut Medicine* devoted to dermatology. The idea came from the Editor, Dr. Louis H. Nahum. Over a year ago Dr. Nahum asked about the desirability of concentrating on a series of papers from one medical specialty. Dr. Sidney N. Klaus took the opportunity to collect six reports from dermatologists, most of whom have, or have had, some affiliation with the Yale Medical School. The topics chosen by Dr. Klaus are varied and show the wide range of present-day dermatology.

Because there is much overlap between disorders of the skin and those of other organs, it is impossible to cover the subject in depth in a small number of articles. One topic of great importance is "Telangiectasia as a Sign of Systemic Disease," by Dr. Irwin Braverman. Dr. Klaus's report on skin color should be read by people within and outside the medical profession. Dr. McDonald discusses mycosis fungoides; Dr. Savin outlines techniques for transplanting hair; Dr. Maibach et al identify the properties of skin responsible for attracting and repelling mosquitos; and Dr. Kugelman explains the diagnosis and treatment of intertrigo. We are grateful that Doctors Klaus and Nahum saw their project through to completion.

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Human Skin in Relationship to Mosquito Attraction and Repulsion

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Introduction

Before the turn of the present century, mosquitoes were studied mainly as objects of natural history observed by curious naturalists. The important discoveries of Manson¹, Ross² and Reed³, however, established mosquitoes as important carriers of human disease. These discoveries lent great impetus to their study not only as vectors of parasites but also as important objects for biological and behavioral studies. A massive scientific literature on the various life aspects of mosquitoes has since accumulated, but their host-seeking behavior remains imperfectly understood.

Host Finding By Mosquitoes

The steps involved in the host-seeking behavior of mosquitoes have been reviewed by Kalmus and Hocking⁴ and more recently by Hocking and Khan⁵.

The adult female mosquito seldom seeks a host soon after emergence. More often she mates and feeds on sugary substance before she is in a proper physiological state to seek a blood meal.⁶⁻⁹ After this period, prior to an urge for a blood meal, the mosquito may take off in response to any specific stimulus such as mechanical disturbance, sight, air movements, host odor, carbon dioxide, or any combination thereof. Except the host odor, other stimuli may not be host induced. The presence of

a host in the vicinity, however, may trigger a positive tactic response towards him. Whether this is induced by odor or merely by heat and moisture is controversial. Some consider heat and moisture to be the only factors responsible for host attraction. Others consider odor more important. The significance of odor in the host-seeking of mosquitoes will be discussed.

As the mosquito closely approaches the host, moisture and warmth become more important in inducing the mosquito to land.¹⁰⁻¹³

After landing the insect selects a suitable site to feed. Tactile and thermal stimuli may play an important role at this stage.⁴ After piercing, the ingestion of blood is determined by the receptors in the food channel.^{14,15} Adenylic acid and its derivatives have been shown to be important in stimulating these receptors.¹⁶⁻¹⁸ Once the mosquito starts its meal it is difficult to dislodge.¹⁹⁻²⁰ This may be due to a rapid increase in the thresholds of stimuli needed for take-off which may, however, soon be decreased by scolopidia registering tension in membranous areas of the integument.⁵

Factors Attractant To Mosquitoes

As we have said, whether or not odor is involved in mosquito attraction is controversial. Wright and Kellogg;²¹ Wright, Daykin and Kellogg²² and Daykin, Kellogg, and Wright²³ find only heat and moisture attractive to mosquitoes. Goeldi²⁴ found sweat attractive but he did not exclude the possible effects of warmth and humidity. Rudolfs²⁵ found sweat or sebaceous secretion somewhat attractive to *Aedes*. Rahm^{26, 27} observed that human sweat may play a part in the attraction of mosquitoes to the human hand and he found olfactory substances of man responsible for greater activity of female *A. aegypti*. Lysine and alanine were reported to be attractive by Brown and Carmichael,^{28, 29} their carbomino compounds by Lipsitz and Brown,³⁰ and the sex hormones or their breakdown products by

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Roessler³¹ and Roessler and Brown.³² Other materials unidentified chemically were found attractive by Shaerffenberg and Kupka^{33,34} and by Van Thiel and Laarman³⁵ and Laarman.³⁶ Clements³⁷ remarks that there is good evidence that odor is important in attraction from a distance. Differences in attractiveness of individuals to *Anopheles* have been demonstrated in the field by Hadow³⁸ Ribbands,³⁹ Muirhead-Thomson⁴⁰ and by Thomas⁴¹ Khan et al.,⁴³ Maibach, Khan and Strauss⁴⁴ and Maibach et al.⁴⁵

Rudolfs²⁵ observed that *Aedes sollicitans* (Walker) and *Aedes cantator* (Coq.) always alighted on the leeward side of a host and could be seen flying upwind towards the host even when a strong wind was blowing. Kennedy⁴⁶ pointed out that mosquitoes downwind could reach the host by wind-borne factors. Bertram and McGregor⁴⁷ report trapping *Anopheles gambiae* Giles and *Anopheles gambiae* var. *melas* Theo. almost exclusively in the leeward entrance trap freed on a baited cattle shed, while no mosquitoes were caught in the unbaited traps.

Another evidence of positive anemotaxis in the presence of human odor was provided recently by Happold⁴⁸ with species of *Aedes* in the field. He used a propeller which directed a wind of 2 m.p.h. over an observer standing 20 ft. up in the forest. After 2 minutes, mosquitoes were flying upwards reaching the 20 ft. platform. A 10 minute control period beforehand yielded no mosquitoes.

In our laboratory, Khan et al.⁴⁹ studied the effect of several stimuli on the approach of *A. aegypti* in a specially constructed tower. The stimuli studied were heat (34°C), water vapor, CO₂, and a combination of these. The human palm was studied as a natural source of attractive stimuli. The approach of mosquitoes to the different stimuli was quantitated and compared for five different heights.

At all heights the number of mosquitoes approaching the palm was maximal compared with other stimuli. With the palm they also came down faster and in maximum number. The number of mosquitoes attracted to the palm rose continuously and steadily with time. They also approached the palm from distances greater than those from which they approached the other stimuli. These observations suggested that heat and moisture may be important to mosquitoes at close proximity, but at greater distance odor seems more important in the hierarchy of attractive stimuli.

Khan and Maibach¹³ further quantitated the effect of several stimuli on the landing and probing

by *A. aegypti* in the same tower. The maximal landings and probings were obtained with the palm. It was concluded that the maximal attraction and the high incidence of landing and probing by *A. aegypti* over the palm was due to some "component" of skin emanation other than heat, moisture or CO₂.

In yet another set of experiments,⁵⁰ the human palm was presented to *A. aegypti* side-by-side with combinations of heat, moisture and several amounts of CO₂ in a large cage dual-port olfactometer. No air-flow was used in this system and the stimuli rose only as convection currents. The objective was to study the effect of various amounts of CO₂ on the behavior of *A. aegypti* and to observe whether heat, moisture, and CO₂, when combined and presented side-by-side with the palm, would confuse the mosquitoes and draw them away from the palm or share the attraction with it. Quite to the contrary, when the palm was so compared, the mosquitoes ignored the heat-moisture-CO₂ combination completely and went to the port with the palm. This confirmed that the attraction to the palm was due to the different nature of the stimuli emanating from it. And the evidence strongly indicated, though still indirectly, that odor is involved in host attraction.

In Search Of Odor Attractive To Mosquitoes

In spite of the overwhelming evidence in support of odor being involved in mosquito attraction, much of this data is indirect. Direct proof of the presence and importance of odor requires first its trapping, and purification and then, in turn, trapping the mosquitoes with it.

To this end we started collecting human arm odor as well as sweat. The odor was collected by passing compressed nitrogen over a forearm in a plastic bag and then trapping the emanations carried by the gas in a dry ice-acetone trap. The sweat was collected by placing a subject in a Sauna bath for one hour, in a large plastic bag. To test sweat or arm odor a dual-port air stream olfactometer was used, described by Skinner et al.⁵¹

In order to select attractive and unattractive subjects for our study, a survey was made to evaluate degrees of attractiveness to mosquitoes in humans. Several hundred human subjects were screened with a biting technique in which mosquitoes were allowed to bite through a screen at the bottom of a small cage placed on the forearm of the subject. Out of 838 individuals tested only one was found who was resistant to mosquito bites. With the probing technique⁴³ we identified a highly attractive

and 3 unattractive individuals from a panel of 100 screened. This method consisted of placing six mosquitoes in a 5 x 5 x 1.5 cm cage made of plexi-glass frame covered on top and bottom with a 20 mesh nylon net. The cage was positioned 1 cm above the forearm of a subject and time was recorded with a stop-watch when half of the mosquitoes (i.e. 3 out of 6) were probing simultaneously on the bottom over the forearm. This was called PT-50, i.e. probing time for 50% of the mosquitoes. The unattractive subjects picked with this technique included the one discovered earlier with the biting technique.

To study the importance of sweat to mosquito attraction *in vivo* we extended the PT-50 study to 2 anhidrotic subjects we had the opportunity to test. The PT-50 on the forearm of these subjects were significantly higher than the PT-50 of the control ($P < 0.01$) but the palm where the subjects sweated was normally attractive.⁴⁵ This study led us to concentrate on sweat more than on the arm air collection. So far our olfactometer studies have shown whole sweat and lyophilized sweat attractive to mosquitoes.⁵¹ The ethanol extracts and ether extracts of the lyophilized sweat have also been found attractive. At present work is in progress on the chromatographic separation of volatile sweat components and their evaluation in the olfactometer.

In Search Of Better Repellents

As the factors attracting mosquitoes to the vertebrate host are poorly understood, so is the mode of action of insect repellents. Repellents are compounds eliciting an avoiding reaction.⁵⁴ How this is actually accomplished by repellent compounds through the neurosensory pathway is little understood; nor do we know what imparts repellent properties to a chemical structure. The bulk of our knowledge on repellents is based on the behavior of whole insects; little has been done on the level of single receptor cells. Almost nothing has been done with mosquitoes specially.

It is known that of the 5 structural types of sensilla on the antennae of *A. aegypti*^{55, 56} A_1 and A_3 types mediate attractancy and the A_2 type mediates repellency.⁵⁵

In the blowfly, the electrophysiological studies of its contact chemoreceptor have shown that when stimuli are applied there is an interaction between activity in the L fibers (mediating electrolyte) and S fibers (mediating sugar).⁵⁷⁻⁵⁹ Hodgson⁵⁷ found that the presence of S impulses is accompanied by a decrease in L impulses and conversely the S

spikes decrease when the L fiber is stimulated. On the same analogy, whether the presence of repellent stimulates the rejection receptors (A_2) in *A. aegypti* accompanied by a simultaneous inhibition of the acceptance receptors (A_1 and A_3) remains to be shown. The repellents inhibiting the receptors for attractancy (A_1 and A_3) directly would obviate the necessity for A_2 receptors, and since economy in functional structure is an important principle of organic evolution, the latter presumption should be incorrect and the former should sound more reasonable even in the absence of direct experimental evidence.

In contrast to repellents affecting A_2 receptors only, Khan²⁰ provided evidence that repellent affect not only the chemoreceptors involved in blood feeding but also other receptors like contact receptors used in the selection of oviposition site, the mechanoreceptors affecting orientation to gravity and air flow, and auditory receptors involved in mating. This study based on behavior suggests that repellents are not receptor-specific but have a broad-spectrum effect involving most receptors except perhaps that of the common chemical sense. The actual nature of interference by repellents in the perception of stimuli by these receptors, however, remains open for investigation.

Coming back to the properties of repellent compounds themselves, with the exception of some correlation between the volatility and repellency,⁶¹ almost nothing is known regarding the physical or chemical makeup impart a compound's repellent properties. Wright^{62, 63} attempted to show that Ramsay's theory⁶⁴ could be used to predict insect repellency from their infra-red absorption spectra. On re-examination, however, Hocking and Khan⁵ did not find a simple or significant correlation between absorption spectra in the range of 449-467 cm^{-1} and repellency that should characterize insect repellents as claimed by Wright.⁶³ The stereochemical theory of olfaction proposed by Amoore⁶⁵⁻⁶⁷ may prove of assistance in the future determination of the olfactory mechanism in insects. An examination of repellent molecules in the light of this theory may give some interesting information, but this possibility remains unexplored so far.

The foregoing account emphasizes our imperfect understanding of the inherent nature of the repellent property and the mode of action of insect repellents. In our experiments with human skin-washings in organic solvents, we found that skin lipids obtained from the washings in acetone or

diethyl ether of the forehead, or arms of humans are usually repellent to female *A. aegypti* when evaluated in a dual-port olfactometer.⁵² The repellent substances could be separated from non-repellent materials present in skin lipids by thin layer chromatography. Only the unsaturated fraction of the hydrocarbon portion of these lipids is responsible in part for the repellency.⁵³ Other more repellent substances present in skin lipids are being chromatographically separated for identification. When lipids were removed from sweat, the attractancy of sweat increased significantly.

Johnson et al⁶¹ prepared a series of ring-substituted N,N-diethylbenzamide analogs of DEET in order to investigate repellent potency in relation to chemical structure and physical properties. A general relationship of repellent potency to volatility was demonstrated. In this series no correlation between repellency and physical properties, such as relative partition coefficient and polarizability, was demonstrated. Some compounds exhibited repellent potencies and duration of effectiveness comparable to those of DEET. Repellent potency, as determined in the olfactometer, did not parallel duration of effectiveness on the skin.

Efforts are being made in our laboratory to understand the loss of repellent compounds from skin surface and to find ways of binding them more cohesively to stratum corneum so that they last longer and resist abrasion better.

Outlook For Developing Better Insect Repellents

Diethyltoluamide (DEET) is the standard topical repellent employed most frequently by the army and by industry. Broadly effective against several species of mosquitoes, its main limitation resides in the requirement for frequent application because of losses due to volatility and abrasion.

With the present state of our knowledge regarding the behavior of blood feeding insects, the factors that attract them to a vertebrate host, the mode of action of insect repellents, and the essential chemical and/or physical factor(s) that would impart repellent properties to a chemical compound, the search for new and better repellents has been through large scale screening of compounds. The discovery of better and more potent repellents through such an approach is inherently more a matter of luck than the fruit of a systematic and scientific approach. It is, therefore, imperative that a more vigorous approach is needed to expand our basic knowledge in the various fields mentioned above. Even then the development of a universal repellent effective against all kinds of blood suck-

ing insects may elude us for a long time to come. Insects vary in their host-seeking behavior not only from species to species, but even at the infra-species level, and any repellent effective against one kind of insect may not be so against another. A topical repellent also suffers from the disadvantages of being affected by all the factors involved in the environment. Heat, moisture in the air, and that given out by the skin, rain, abrasion, absorption through the skin, etc., the protection time of any repellent is, therefore, bound to vary from place to place and from subject to subject. In addition, the demand of consumer acceptability based on factors like smell, cutaneous or mucous membranes, irritation, and staining narrows down the choice of effective repellents. Under the circumstances, while we make deeper inroads in the fields of host attractancy, insect behavior and the mode of action of repellent chemicals, it is worthwhile to search for new repellents by screening new compounds as well as to improve the existing ones. A long-acting, orally ingested repellent would be the ideal solution to the problem. A scientific search for such a compound constitutes a challenge to research in this field.

References

1. Manson, P. On the development of *Filaria sanguinis hominis* and on the mosquito considered as a nurse. J. Linn. Soc. (Zool.) 14:304-11, 1879.
2. Ross, R. Report on the cultivation of *Proteosoma* Labbe in grey mosquitoes. Indian Med. Gaz. 33:173-5, 401-8, 448-51, 1898.
3. Reed, W., Carroll, J., Agramonte, A., and Lazear, J. W. The etiology of yellow fever. A preliminary note. Phila. Med. J. 6:790-796, 1900.
4. Kalmus, H., and Hocking, B. Behavior of *Aedes* mosquitoes in relation to blood-feeding and repellents. Entomologia exp. appl. 3:1-26, 1960.
5. Hocking, B., and Khan, A. A.: The mode of action of repellent chemicals against blood-sucking flies. Canad. Ent. 98:821-831, 1966.
6. Seaton, D. R., and Lumsden, W. H. R. Observations on the effect of age, fertilization and light on biting by *Aedes aegypti* in a controlled microclimate. Ann. Trop. Med. Parasit. 35:23-36, 1941.
7. Hocking, B., Richards, W. R., and Twinn, C. R. Observations on the bionomics of some northern mosquito species (Culicidae: Diptera). Canad. J. Res. D. 28:58-80, 1950.
8. Gillett, J. D., Haddow, A. J., and Corbet, P. S. The sugar feeding cycle in a cage population of mosquitoes. Entomologia exp. appl. 5:223-232, 1962.
9. Strauss, W. G., Maibach, H. I., Khan, A. A., and Pearson, T. R. Observations on biting behavior of *Aedes aegypti* (L.). Mosquito News 25:272-275, 1965.
10. Howlett, F. M. The influence of temperature upon the biting of mosquitoes. Parasitology 2:479-484, 1910.
11. Marchand, W. Thermotropism in insects. Ent. News 31:159-165, 1920.

12. Brown, A. W. A., Factors in the attractiveness of bodies for mosquitoes. *Nature*, London 167:202, 1951.
13. Khan, A. A., and Maibach, H. I. Quantitation of effect of several stimuli on landing and probing by *Aedes aegypti*. *J. Econ. Entom.* 59:902-905, 1966.
14. Trembley, H. L. The distribution of certain liquids in the aesophageal diverticula and stomach of mosquitoes. *Am. J. Trop. Med. Hyg.* 1:693-710, 1952.
15. Salama, H. S. The function of mosquito taste receptors. *J. Insect Physiol.* 12:1051-1060, 1966.
16. Hosoi, T. Identification of blood components which induce gorging of the mosquito, *J. Ins. Physiol.* 3:191-218, 1959.
17. Smith, C. N., Gilbert, I. H., and Gouck, H. K.: Factors in the attraction of mosquitoes to hosts, and their relation to protection with repellents. *Proc. XI. Inter. Cong. Ent.* (Vienna, 1960), Symp. V 3:82, 1962.
18. Galun, R., Avid-Doz, Y., and Bar-Zeev, M. Feeding response in *Aedes aegypti*. Stimulation by adenosine triphosphate. *Science* 142:1674-1675, 1963.
19. Christophers, S. R. *Aedes aegypti* (L.) the yellow Fever Mosquito. The University Press, Cambridge, 1960.
20. Khan, A. A. Effects of repellents on mosquito behavior. *Quaest. ent.* 1:1-35, 1965.
21. Wright, R. H., and Kellogg, F. E. Response of *Aedes aegypti* to moist convection currents. *Nature*, London 194:402-403, 1962.
22. Wright, R. H., Daykin, P. N., and Kellogg, F. E. Reaction of flying mosquitoes to various stimuli. *Proc. XII int. Congr. Ent.*, London (1964) 281-282, 1965.
23. Daykin, P. N., Kellogg, F. E., and Wright, R. H. Host-finding and repulsion of *Aedes aegypti*. *Canad. Ent.* 97:239-263, 1965.
24. Goeldi, E. A. Os mosquito no Para. *Mem. Mus. Goeldi* (Paraense), No. IV, 1905.
25. Rudolfs, W. Chemotropism of mosquitoes. *N. J. Agric. Exp. Sta. Bull.* No. 367, pp. 1-23, 1922.
26. Rahm, U. Zur Bedeutung des Duftes und des Schweisses bei der Attraktion von *Aedes aegypti* durch en Menschen. *Acta trop.* 14:208-217, 1957.
27. Rahm, U. Die attraktive Wirkung der vom Menschen abgegebenen Duftstoffe auf *Aedes aegypti* L. *Z. Tropenmed. u. Parasit.* 9:146-156, 1958.
28. Brown, A. W. A., and Carmichael, A. G. Lysine as a mosquito attractant. *Nature*, London 189:508-509, 1961a.
29. Brown, A. W. A., and Carmichael, A. G. Lysine and alanine as mosquito attractants. *J. Econ. Entomol.* 54:317-324, 1961b.
30. Lipsitz, E. Y., and Brown, A. W. A. Studies on the responses of the female *Aedes* mosquito, IX. The mode of attractiveness of lysine and other amino-acids. *Bull. Ent. Res.* 54:675-687, 1964.
31. Roessler, P. The attractiveness of steroids and amino acids to female *Aedes aegypti*. *Proc. 50th Annual Meeting N. J. Mosq. Exterm. Assoc.* pp. 250-255, 1963.
32. Roessler, P., and Brown, A. W. A. Studies on the responses of the female *Aedes* mosquito, X. Comparison of oestrogens and amino acids as attractants. *Bull. Ent. Res.* 55:395-403, 1964.
33. Shaefferberg, B., and Kupka, H. Untersuchungen über die geruchliche blutsaugende Insekten, I. Über die Wirkung eines Blutduftstoffes auf *Stomox* und *Culex*. *Öst. Zool. Z.* 3:410-424, 1951.
34. Shaefferberg, B., and Kupka, H. Der attraktive Factors des Blutes für blutsaugende Insekten. *Naturwissenschaften* 46:457-458, 1959.
35. Van Thiel, P. H., and Laarman, J. J. What are the reactions by which the female *Anopheles* finds its blood supplier? *Docum. Med. geogr. Trop.* 6:156-161, 1953.
36. Laarman, J. J. The host-seeking behavior of the malaria mosquito *Anopheles maculipennis atroparvus*. *Acta Leidensia* 25:1-144, 1955.
37. Clements, A. N. *The Physiology of Mosquitoes*. The Macmillan Co., New York, 1963.
38. Haddow, A. J. The mosquito fauna and climate of native huts at Kisumu, Kenya. *Bull. Ent. Res.* 33:91-142, 1942.
39. Ribbands, C. R. Studies on the attractiveness of human populations to anopelins. *Bull. Ent. Res.* 40:227-238, 1949.
40. Muirhead-Thomson, R. C. The distribution of anopheline mosquito bites among different age-groups. A new factor in malaria epidemiology. *Brit. Med. J.* 1:1114-1117, 1951.
41. Thomas, T. C. E. Biting activity of *Anopheles gambiae*. *Brit. Med. J.* 2:1402, 1951.
42. Freyvogel, T. A. Ein Beitrag zu den Problemen um die Blutmahlzeit von Stechmücken, *Acta Trop.*, Basel 18:201-251, 1961.
43. Khan, A. A., Maibach, H. I., Strauss, W. G., and Fenley, W. R. Screening humans for degree of attractiveness to mosquitoes. *J. Econ. Entom.* 58:694-697, 1965.
44. Maibach, H. I., Khan, A. A., and Strauss, W. G. Attraction of humans of different age groups to mosquitoes. *J. Econ. Entom.* 59:1302-1303, 1966.
45. Maibach, H. I., Khan, A. A., Strauss, W. G., and Pearson, T. R. Attraction of anhidrotic subjects to mosquitoes. *Arch. Derm.* 94:215-217, 1966.
46. Kennedy, J. S. The visual responses of flying mosquitoes. *Proc. Zool. Soc. London (A.)* 109:221-242, 1939.
47. Bertram, D. S., and McGregor, I. A. Catches in the Gambia, West Africa, of *Anopheles gambiae* Giles and *A. gambiae* var. *melas* Theobald in entrance traps of a baited portable wooden hut, with special reference to the effect of wind direction. *Butt. Ent. Res.* 47:669-681, 1956.
48. Happold, D. C. D. Mosquito ecology in Central Alberta, II. Adult population and activities. *Canad. J. Zool.* 43:821-846, 1965.
49. Khan, A. A., Maibach, H. I., Strauss, W. G., and Fenley, W. R. Quantitation of effect of several stimuli on the approach of *Aedes aegypti*. *J. Econ. Entom.* 59:690-694, 1966.
50. Khan, A. A., Strauss, W. G., Maibach, H. I., and Fenley, W. R. Comparison of the attractiveness of the human palm and other stimuli to the Yellowfever mosquito. *J. Econ. Entom.* 60:318-320, 1967.
51. Skinner, W. A., Tong, H., Pearson, T., Strauss, W. G., and Maibach, H. I.: Human sweat components attractive to mosquitoes. *Nature* 207:661-662, 1965.
52. Skinner, W. A., Tong, H., Maibach, H. I., Khan, A. A., and Pearson, T. Repellency of skin surface lipids of humans. *Science* 149(3681):305, 1965.
53. Skinner, W. A., Tong, H. C., Pearson, T. R., and Maibach, H. I. Repellency of human skin-surface lipid hydrocarbons to the yellow-fever mosquito. *J. Econ. Entom.* 60:927-929, 1967.
54. Dethier, V. G. Repellents. *Annual Rev. Ent.* 1:181-202, 1956.
55. Slifer, E. H., and Sekhon, S. S. The fine structure of the sense organs as the antennal flagellum of the yellow fever mosquito, *Aedes aegypti* L. *J. Morph.* 111:49-68, 1962.

56. Steward, C. C., and Atwood, C. E. The sensory organs of the mosquito antenna. *Canad. J. Zool.* 41:557-594, 1963.
57. Hodgson, E. S., and Roeder, K. D. Electrophysiological studies of arthropod chemoreception, I. General properties of the labellar chemoreceptors of Diptera. *J. Cell Comp. Physiol.* 48:51-76, 1956.
58. Morita, H. Initiation of spike potentials in contact chemosensory hairs of insects, III. D. C. stimulation and generator potential of labellar chemoreceptor of *Calliphora*. *J. Cell. Comp. Physiol.* 54:189-204, 1959.
59. Sturckow, B. Über den Geschmackssinn und den Tastsinn von *Leptinotarsa decemlineata* Say (Chrysomelidae). *Z. vergl. Physiol.* 42:255-302, 1959.
60. Hodgson, E. S. Electrophysiological studies of arthropod chemoreception, II. Responses of labellar chemoreceptors of the blowfly to stimulation by carbohydrates. *J. Ins. Physiol.* 1:240-247, 1957.
61. Johnson, H. L., Skinner, W. A., Maibach, H. I., and Pearson, T. R. Repellent activity and physical properties of ring-substituted N,N-diethyl benzamides. *J. Econ. Entom.* 60:173-176, 1967.
62. Wright, R. H. Physical basis of insect repellency. *Nature, London* 178:638, 1956.
63. Wright, R. H. A theory of olfaction and of the action of mosquito repellents. *Canad. Ent.* 89:518-528, 1957.
64. Ramsay, W. On smell. *Nature, London* 26:187-189, 1882.
65. Amoore, J. E. Elucidation of the stereochemical properties of the olfactory receptor sites. *Proc. Toilet Goods Assoc., Sci. Sect., No. 37 (Suppli)*, 1962, p. 13.
66. Amoore, J. E. Stereochemical theory of olfaction. *Nature* 198:271, 1963.
67. Amoore, J. E. Stereochemical theory of olfaction. *Nature* 199:912, 1963.

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Intertrigo—Diagnosis and Treatment

Thomas P. Kugelman, M.D.

Intertriginous eruptions all manifest the effects of heat, moisture, friction, and maceration produced by the frequent and prolonged apposition of two adjacent skin surfaces. The axillae, inframammary folds, umbilicus, groins, intergluteal cleft, and interdigital webs are the areas most commonly involved, but in obese individuals additional redundant folds of skin may be subject to the same pathology. Some diseases, such as psoriasis, occur in intertriginous areas only fortuitously; others, like candidiasis, depend upon the environmental conditions prevalent there. In either case, however, the persistent moisture and maceration modify the morphology of lesions, obscure characteristic signs, and often produce a nondiagnostic clinical picture.

In the past, therapeutic efforts were directed largely at restoring to normal the altered environment present in intertrigo. While this approach is still necessary and useful, the advent of corticosteroids and antibiotics has made more specific and sophisticated treatment possible. The effective use of these agents makes an accurate etiologic diagnosis mandatory. This paper will present briefly the differentiating features of skin diseases of similar morphology involving intertriginous areas.

For convenience, the diseases to be considered will be grouped as follows:

Infections

- Candidiasis (Moniliasis)
- Dermatophytosis (Tinea, ringworm)
- Erythrasma
- Pyoderma

Non-infectious Inflammatory Diseases

- Miliaria (Intertrigo)
- Fox-Fordyce Disease
- Contact Dermatitis
- Atopic Dermatitis
- "Neurodermatitis"
- Psoriasis
- Seborrheic Dermatitis
- Pemphigus

Non-inflammatory Diseases

- Lichen Sclerosus et Atrophicus
- Acanthosis Nigricans

Neoplasms

- Superficial Basal Cell Epithelioma
- Bowen's Disease
- Paget's Disease

Infections

This group includes the most common intertriginous disorders affecting the post-pubertal age group. The groins and toeweb are most frequently infected. Identification of a causative organism is of the utmost importance since available antibiotics are effective against only one class of organisms. Culture, Wood's light illumination, and direct microscopic examination of scale or exudate from the lesions immersed in 10% KOH are the appropriate diagnostic procedures.

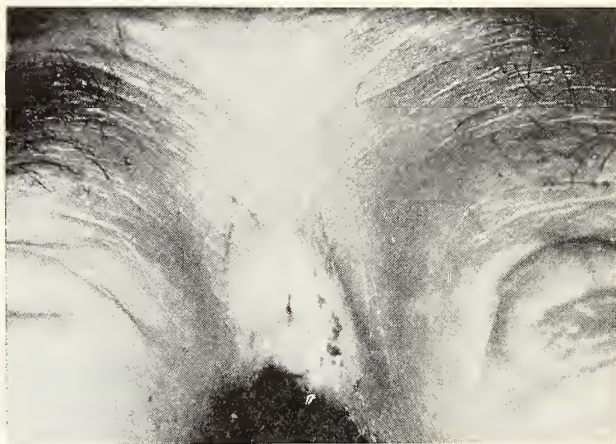


Figure 1

Candidiasis of interdigital web between second and third fingers (erosio interdigitalis). Sharp margination, maceration, and whitish exudate are evident.

Candidiasis (Fig. 1).—Most "true" intertrigo results from either primary or secondary infection with the ubiquitous organism *Candida albicans*. Intensely pruritic, diffusely erythematous, and sharply marginated plaques appear quite suddenly. "Satellite pustules" often appear around the periphery. A variable amount of whitish exudate is usually present, although lesions may also be dry, scaly, or erosive. Lesions on the mucous membranes or scrotum help confirm the diagnosis. Since *Candida* organisms are frequently present as saprophytes on normal mucous membrane and moist skin, a positive culture alone is insufficient proof of diagnosis. This must be accompanied by the find-

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ing of the invasive mycelial phase of the organism on microscopic examination of scrapings from the lesion. The slender branching hyphae with clusters of spores are best seen in acute exudative lesions. The presence of candidiasis should always alert the physician to the possibility of underlying endocrinopathy or debilitating disease.

The only effective antibiotic for the systemic treatment of candidiasis is amphotericin B (Fungizone), which must be given intravenously and is too nephrotoxic for routine use.¹ Oral preparations of nystatin (Mycostatin) and amphotericin B are not appreciably absorbed and are useful only for gastrointestinal candidiasis. Both drugs are very effective topically, however, with a low incidence of resistant organisms, allergic hypersensitivity, or primary irritation. Nystatin is the more widely used and has been incorporated into a number of combinations with other antibiotics and corticosteroids (Mycolog, Nystaform-HC, Neo-Nysta-Cort, Achrostatin V, etc.). The availability of creams, ointments, lotions, powders, oral suspensions and vaginal suppositories permits the selection of an appropriate vehicle. Combinations, such as Mycolog (nystatin, neomycin, gramicidin, and triamcinolone), are effective but should be prescribed only for limited periods because of the sensitizing potential of neomycin and the dermal atrophy produced by long-term use of topical steroids.² Infections will usually respond in a few days, but to prevent recurrences, treatment is best continued until tissue healing is complete. Chlordantoin (Sporostacin) and older remedies such as gentian violet and iodochlorhydroxyquin (Vioform) are effective alternatives but less convenient to use.

Dermatophytosis.—Intertriginous infections in the Northeastern U.S. are usually caused by *Trichophyton rubrum*, *T. mentagrophytes*, or *Epidermophyton floccosum*. Adult males are most frequently involved. Tinea cruris is characterized by pruritic erythematous scaling plaques on the upper medial thighs. The plaques show a circinate advancing border and a tendency to central clearing. The scrotum and glans penis are usually not affected. Dermatophytosis, especially when caused by *T. rubrum*, tends to be less acute and of longer duration than candidiasis. In tinea pedis, the third and fourth interspaces usually show fissuring, maceration, and pruritus. The nails and soles may also be infected. Asymmetry of involvement is often striking. Septate branching hyphae in KOH preparations (Fig. 2) and positive cultures on Sabour-

aud's agar confirm the diagnosis. There is usually no fluorescence under a Wood's light.



Figure 2

High power appearance of *T. rubrum* hyphae in KOH preparation of scale. Note branching and septations. Compare size relative to underlying epidermal cells.

Griseofulvin (Fulvicin-U/F, Grifulvin V, Grifolvin V) is the only effective systemic antibiotic. Daily doses of 0.5-1.0 Gm. of the microcrystalline type are required for a period of three to four weeks. Headaches and gastrointestinal upsets are common side effects, but these usually disappear spontaneously with continuation of therapy. Photosensitivity, leukopenia, hypersensitivity reactions, and psychomotor disturbances have been reported but are rare. Although griseofulvin is derived from a species of *Penicillium*, cross-sensitivity with penicillin does not usually occur. Tolnaftate (Tinactin) is an effective and non-irritating topical agent which is far superior to previously available agents containing undecylenic, salicylic, and benzoic acids, which were of little use in inflammatory intertriginous infections. *T. rubrum* infections may be refractory to all available forms of therapy, and recurrences are common in successfully treated cases.

Erythrasma (Fig. 3).—The etiologic agent of this infection, long considered to be a fungus, is now known to be *Corynebacterium minutissimum*, a Gram-positive rod which produces a fluorescent reddish pigment visible under Wood's light. It has been reported to occur in the genitocrural area and toeweb of 25% of normal adult males,³ but the majority of these infections are asymptomatic and clinically unrecognized. Sharply marginated dry dull red scaling plaques appear on the medial thighs, especially the area in contact with the scrotum. The axillae, toeweb and perianal area may be similarly involved. Pruritus is variable but may be intense. The diagnosis is most readily made by looking for coral red fluorescence under the Wood's light. Errors may result if the patient has applied a fluorescent topical medication or if vigorous washing just prior to his visit has removed the pigment produced by the organism. Examination of Gram-stained preparations under the oil immersion lens, and culture on special bacteriologic media are useful in doubtful cases.

Erythromycin, administered systemically for five or more days, is the most widely used treatment. Broad spectrum antibiotics are also effective, but topical antibiotics provide only temporary suppression of the infection. Toeweb infections are especially prone to recur and need not be treated if asymptomatic.

Pyodermas.—Coagulase-positive staphylococci and beta-hemolytic streptococci cause the great majority

of pyodermas. Staphylococcal folliculitis and furunculosis are common in the axilla and groin, and may become chronic. This must be differentiated from hidradenitis suppurativa, a chronic and recurrent apocrine gland disorder characterized by deep tender nodules, cysts, and communicating sinus tracts that tend to break down, ulcerate, and drain. Pyogenic organisms are often isolated from such lesions, but since the disease is caused primarily by follicular occlusion, antimicrobial therapy is only partially effective.

Both staphylococci and streptococci cause cellulitis which may be primary or superimposed upon a pre-existing disease. Rapidly advancing, bright red, edematous, and well demarcated plaques from which streptococci are isolated are called erysipelas. These infections can usually be differentiated from other disorders by the greater degree of inflammation, adenopathy, and constitutional reaction. Superficial "honey-colored" crusted lesions (impetigo) usually cause no systemic reaction.

Penicillin or other appropriate antibiotics given systemically are the most effective treatment. Such therapy is indicated because of the occasional occurrence of post-streptococcal glomerulonephritis or rheumatic fever. Topical antibiotics are of value mainly in very superficial impetiginous infections. Many effective ones are available, including bacitracin, neomycin, gramicidin, polymixin, and various combinations of these. Neomycin is the most

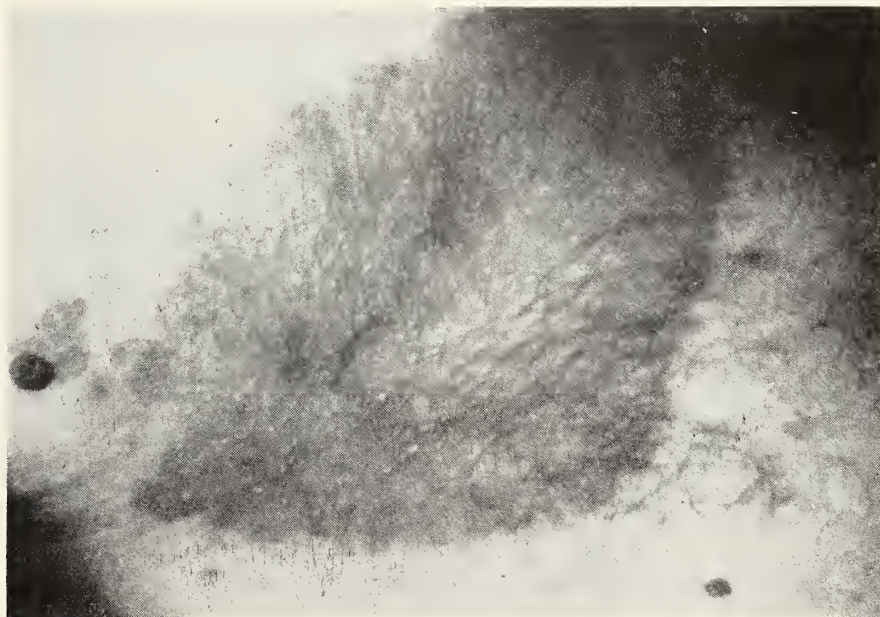


Figure 3

Erythrasma of axilla, showing sharp margins, lack of exudate or scale, and involvement of vault.

widely used but has considerable sensitizing potential. Gentamicin (Garamycin) is a new and effective addition to the group.

Non-Infectious Inflammatory Diseases

The clinical manifestations of the eruptions comprising this group are often similar to one another and to those of the preceding group. Since there is no exogenous causative agent, greater attention must be given to details of history, distribution of lesions, and morphology. A specific diagnosis, especially in the case of allergic hypersensitivity, is no less important for rational management. These diseases share their beneficial response to the anti-inflammatory effects of corticosteroids.

Miliaria.—Miliaria is the inflammatory response of the skin resulting from occlusion of eccrine sweat ducts and extravasation of sweat into deeper layers of the skin. Its occurrence requires the right combination of heat, sweat, salt concentration, and, possibly, the presence of staphylococci. The term "intertrigo," when used to connote a specific entity, may be considered a form of miliaria, modified by the macerating effect of apposing skin surfaces. The skin folds show erythema, edema, and exudation, often with the characteristic odor of decomposed sweat. Creases within an intertriginous area usually respond with greater intensity. Papules and pustules, characteristic of miliaria elsewhere, are not prominent.

Fox-Fordyce Disease.—This rare dermatosis occurs mostly in women and consists of intensely pruritic perifollicular papules in the axillae, pubic region, and on the nipples. It may be a form of "apocrine miliaria," that is, a disease of poral occlusion of the apocrine sweat ducts. Endocrine factors appear to influence its course, since beneficial effects have followed pregnancy and the administration of oral contraceptives.⁴

Contact Dermatitis.—Contact dermatitis represents the reaction of the skin to the direct application of chemical irritants (primary irritant type) or sensitizing agents (allergic type). The enhanced permeability of intertriginous skin increases its susceptibility to both types. Knowledge of common offending substances and their characteristic distribution patterns will facilitate an accurate diagnosis.

Diaper rash is the most common form of primary irritant dermatitis, although the precise nature of the ingredients of urine and feces which produce the dermatitis is still in dispute. Ammonia is often

incriminated. The degree of involvement ranges from simple erythema over the perineum to a severe erosive and ulcerative dermatitis involving the entire diaper area. Secondary candidiasis and pyodermas often supervene. Frequent diaper changes, cleanliness, dryness, avoidance of occlusive rubber or plastic pants, and applications of bland protective agents, such as zinc oxide ointment, are basic to successful management. The anti-inflammatory effect of a topical steroid and specific antimicrobial therapy may be indicated in severe or refractory cases.

In adults, contact dermatitis is more often of allergic than irritant etiology. Common causes include:⁵

Clothing

- Rubber (girdles, brassieres, shorts, shoes)
- Dyes (furs, leather, occasionally other garments)
- Chemical finishes (wrinkle free, permanent press)

Topical Medications

- Anesthetics ("caine" preparations)
- Antibiotics (neomycin, nitrofurazone [Furacin], sulfonamides, penicillin)
- Antiseptics (mercurials, bithionol, hexachlorophene, scarlet red)
- Antihistamines

Cosmetics

- Hair dye (paraphenylene diamine)
- Antiperspirants and deodorants (usually primary irritants)
- Perfumes
- Lanolin
- Depilatories

Allergic hypersensitivity can be confirmed by patch testing. Appropriate concentrations of the suspected allergens are applied to an uninvolved area of skin and the results observed 48 hours later.

Sensitizing agents are frequently transferred by the hands to the face and perineum. The scalp, palms, soles, and vault of the axilla remain unaffected. Erythema, edema, weeping, vesiculation, and intense pruritus characterize the eruption. Elimination of the offending agent and use of topical or systemic corticosteroids provide rapid resolution of the dermatitis.

Atopic Dermatitis and Localized Neurodermatitis (Lichen Simplex Chronicus).—Atopic eczema is a manifestation of a hereditary constitutional dis-

order affecting basic immunologic responses and multiple tissue sites. Although primarily a disease of children, it occurs also in adults. The skin of atopic individuals is dry, pruritic, and sensitive to primary irritants, wool, and certain allergens such as nickel and neomycin. Emotional stress, extremes in temperature and humidity, friction, and sweating may cause exacerbations. The disease shows predilection for the flexural areas. Chronicity is the rule and results in lichenification and hyperpigmentation. Associated findings such as the delayed blanch response to injection of acetyl choline, polysensitivity to scratch tests, allergic rhinitis, asthma, and positive family history help establish the diagnosis.

Localized neurodermatitis (lichen simplex) is seen most commonly, but not exclusively, in atopic individuals. Erythema, scaling, excoriation, and lichenification are the prominent features. The scrotum, vulva, and peri-anal skin are common sites. Psychosexual conflicts are often implicated.

Removal of known aggravating factors, appropriate emollients, and topical or systemic corticosteroids will usually produce remission. The use of potentially irritating or sensitizing agents must be scrupulously avoided.

Seborrheic Dermatitis and Psoriasis (Fig. 4).—These two conditions are often indistinguishable from one another when occurring in intertriginous areas and may, in fact, coexist in the same patient. More or less symmetrical, sharply defined erythematous plaques appear, often lacking the characteristic scale seen elsewhere. Involvement of the scalp, nails, face or other areas will help to establish the correct diagnosis.



Figure 4

Seborrheic Dermatitis involving neck, anterior chest, and axilla demonstrating poorly defined borders and lichenification.

Topical steroids usually provide rapid remissions, but recurrences frequently follow when treatment is discontinued prematurely. Simultaneous treatment of other lesions is essential. Sulfur in various forms for seborrheic dermatitis, and coal tar extracts and salicylic acid for psoriasis are useful adjuncts in therapy. Both diseases improve with sunlight and ultraviolet light. Methotrexate is effective systemically in severe intractable psoriasis.⁶ Systemic corticosteroids are not ordinarily used in these conditions because of severe "rebound" when they are discontinued.

Pemphigus.—Intertriginous pemphigus occurs in two distinct and unrelated forms—pemphigus vegetans and familial benign chronic pemphigus (Hailey and Hailey). Both are rare. The former is a form of pemphigus vulgaris, characteristically limited to the mouth and intertriginous areas, where deep seated large vegetative lesions develop. The prognosis is the same as for pemphigus vulgaris, and vigorous treatment with systemic corticosteroids is indicated. Permanent remissions following such therapy have been reported.

Hailey-Hailey disease, while showing the microscopic epidermal changes of acantholysis common to other types of pemphigus, is a separate entity. It runs a chronic benign course and is characterized by the recurrent appearance of superficial bullae on the neck and other intertriginous areas which become eroded and crusted. It responds well to systemic antibiotics, suggesting that pyogenic organisms play a role in the genesis of the lesions.

Non-Inflammatory Diseases

A number of rare but distinctive diseases are included here. They are usually readily distinguished from those previously considered on clinical or histologic grounds. Only those bearing superficial resemblance to intertrigo will be briefly mentioned. As a group they tend to be chronic, progressive, and unresponsive to currently available therapy.

Lichen Sclerosus et Atrophicus.—The primary lesions are atrophic white flat-topped papules which coalesce to form sclerotic plaques. The surface of plaques shows cigarette paper-like wrinkling and "delling" or central depression. Although most commonly seen on the neck and upper trunk in older women, it occurs in both sexes at all ages. Many consider kraurosis vulvae and balanitis xerotica obliterans to be genital manifestations of this disorder. Early kraurosis vulvae may manifest erythema and edema with intense pruritus, making

a distinction from other types of inflammatory vulvitis difficult. Biopsy is usually diagnostic. Differentiation from leukoplakic vulvitis is essential, since kraurosis vulvae is *not* premalignant but tends to recur following surgery or radiation therapy. Topical steroids may afford some relief of pruritus.

Acanthosis Nigricans.—Asymptomatic hyperpigmented verrucous or papillomatous plaques develop in the folds of the neck, axillae, and groins. The adult form of the disease is almost invariably associated with a visceral malignancy, usually an adenocarcinoma. A benign form also exists, usually associated with obesity or an endocrinopathy. The disease is asymptomatic, but its appearance requires intensive search for the underlying cause. The lesions tend to regress when this is removed.

Neoplasms

Only those tumors which have morphologic similarities to previously discussed disorders will be mentioned. Although not common, their existence must be kept in mind and a biopsy performed in any refractory lesion. They are clinically similar to one another and may mimic psoriasis closely.

Superficial Basal Cell Epithelioma.—Not to be confused with the more common nodular or "rodent ulcer" forms, those lesions usually appear as multiple asymptomatic sharply margined dull red plaques. A fine "threadlike" elevated border is characteristic. Lesions rarely become invasive but enlarge peripherally and may ulcerate. Ingestion of inorganic arsenic has been incriminated in some cases. The superficial nature and large size of these lesions usually makes electrodesiccation and curettage the treatment of choice. Extensive full thickness grafting can often be avoided by this means. The cure rate approaches 100% in adequately treated cases. Recently, the topical use of the antimetabolite⁶ 5-fluoro-uracil has been introduced, but its value in the treatment of malignancies remains to be proven.

Bowen's Disease (Fig. 5).—Microscopically, an intraepidermal squamous cell carcinoma, these lesions are difficult to distinguish morphologically from superficial basal cell epitheliomata; they usually lack the elevated border and are more often single. They rarely become invasive but are of great significance since *one third or more* of these patients develop underlying visceral malignancies.⁷ A full annual cancer workup is indicated for every

patient in whom this diagnosis is made. Treatment is the same as for superficial basal cell epithelioma.



Figure 5

Perianal Bowen's Disease surrounding hemorrhoidal tag. Lesion is bilateral but asymmetrical and covered with white scale.

Paget's Disease.—Non-healing eczematous-looking lesions on the nipples or other apocrine gland regions (axillae, pubic area) should be suspected of being Paget's Disease until proven otherwise. They are almost always extensions of an underlying intraductal carcinoma. Erythema, induration, and some scaling or crusting are the presenting symptoms. Men as well as women are affected. Simple mastectomy or other appropriate excisional surgery is indicated.

General Treatment Of Intertriginous Eruptions

Since heat, sweat, friction, maceration and altered microbial flora are common to all diseases affecting intertriginous areas, certain general therapeutic measures are applicable, regardless of etiology. Every effort must be made to restore a normal environment that will encourage the great natural regenerative capacity of the skin.

TABLE I
DIFFERENTIAL DIAGNOSIS AND TREATMENT OF COMMON INTERTRIGINOUS ERUPTIONS

Disease	Etiology	Diagnostic Tests	Other Sites of Involvement	Predisposing Factors	Therapy
<i>Infectious</i>					
Candidiasis	C. albicans	KOH and culture	Mucous membranes, nails, viscera	Diabetes, hypoparathyroidism, antibiotics (S), corticosteroids (S), pregnancy	Nystatin (T) Amphotericin B (T & S) Clordantoin (T)
Dermatophytosis (ringworm, tinea)	T. rubrum T. mentag. E. floccosum	KOH and culture	Palms and soles, nails, other glabrous skin	Hyperadrenocorticism	Griseofulvin (S) Tolnaftate (T)
Erythrasma	C. minutissimum	Wood's light, culture	Glabrous skin (rare)		Erythromycin (S) Other antibiotics
Pyoderma (cellulitis, erysipelas, folliculitis)	S. aureus, beta-hemolytic streptococcus	Smear and culture	Any organ	Debilitation, hypogammaglobulinemia, others?	Penicillin, other antibiotics (S), neomycin, bacitracin, gentamicin, gramicidin, etc. (T)
<i>Inflammatory</i>					
Miliaria	Eccrine duct occlusion		Glabrous skin	Profuse sweating, ↑ NaCl concentration	Cool environment, washing
Contact dermatitis (diaper rash)	Primary irritants, allergens	Patch tests (suspected allergens)	Other areas of contact	Atopy, pre-existing skin disease	Avoidance of irritants, steroids (T & S)
Atopic dermatitis	Hereditary	White dermographism, polysensitivity to scratch tests (non-specific), etc.	Face, hands etc. (hay fever, asthma)	Irritants, emotional stress, wool, heat, cold, etc.	Avoidance of irritants, steroids (T & S), ultraviolet light
Psoriasis	Unknown (hereditary)	Biopsy	Scalp, nails, extensor surfaces, etc., joints (10%)	Trauma (Koebner), emotional stress	Ultraviolet light, steroids (T) methotrexate (S), other agents
Seborrheic dermatitis	Unknown		Scalp, face, ears	Emotional stress	Ultraviolet light, steroids (T), sulfur preparations (T)

(S)—Systemic medication; (T)—Topical medication

Weeping lesions should be treated with intermittent cool or lukewarm compresses, using tap water or Burow's Solution 1:20, followed by air-, lamp-, or fan-drying of affected areas. Plain talcum powder may be used to absorb moisture and proper supportive garments worn to reduce apposition of skin surfaces. Cotton is the most suitable fabric; wool should be avoided. Lotions and vanishing creams, containing only necessary ingredients, are preferable to greasy ointments which may promote sweat retention. Potentially irritating or sensitizing medications must be strictly avoided. 3% Iodo-chlorhydroxyquin (Vioform) lotion or cream may be used where broad bacteriostatic and fungistatic effects are desired. Topical steroids are generally safe for relief of inflammation and pruritus. Weight reduction and scrupulous hygiene are important preventive measures. In every case, treatment should be continued until the skin is fully healed to prevent recurrences, but the prophylactic use of steroids or antibiotics should be discouraged.

Comment

It is apparent that the rational management of intertrigo in this sophisticated era of antibiotics, corticosteroids, and cancer chemotherapeutic agents depends upon accurate diagnosis. This is further necessitated by the knowledge that several of the diseases are associated with an underlying endocrinopathy or malignancy. Candidiasis is a well known manifestation of diabetes, hypoparathyroidism, pregnancy, and systemic steroid or antibiotic therapy. Dermatophytosis may indicate hyperadrenocorticism. Recurrent pyoderma suggests hypogammaglobulinemia. Atopic dermatitis is associated with anaphylactoid reactions, migraine headaches, etc. Psoriatic patients may develop a severe mutilating arthritis. Acanthosis nigricans, Bowen's Disease, and Paget's Disease all demand a search for an underlying malignancy. Obviously the con- with cataracts, a flat glucose tolerance curve, po-

scientious physician must consider these ramifications of apparently simple problems.

The diagnostic tools required to differentiate among the diseases described here are simple and easily available. A microscope for examination of parasites, scale or exudate; a Wood's lamp for the identification of fluorescent organisms; Sabouraud's agar for cultures; a patch-testing kit for screening common allergens; and a biopsy punch are all that are needed. Finally, a careful history and examination of the entire body surface—especially the scalp, hands, and feet—will often provide the necessary clues for an astute diagnosis.

Table I summarizes the pertinent information.

Summary

Intertriginous skin eruptions are due to a number of specific microbial, allergic, neoplastic, hereditary, and acquired etiologic factors. Some are confined to these areas; others appear there fortuitously. Their morphologic similarity results from the macerating effect of heat, moisture, and friction between apposing skin surfaces. The large number of new specific therapeutic agents and the regular occurrence of serious underlying systemic diseases make exact diagnosis and treatment essential.

References

1. Hildick-Smith, G., Blank, H., and Sarkany, I.: Fungus Diseases and Their Treatment. Boston, Little, Brown & Co., 1964.
2. Epstein, N. N., Epstein, W. L., and Epstein, J. H.: Atrophic striae in patients with inguinal intertrigo. *Arch. Derm.* 87: 450-457, 1963.
3. Sarkany, L., Taplin, D., and Blank, H.: Incidence and bacteriology of erythrasma. *Arch. Derm.* 85: 578-582, 1962.
4. Kronthal, H. L., Pomeranz, J. R., and Stomer, G.: Fox-Fordyce Disease. *Arch. Derm.* 91: 243-245, 1965.
5. Fisher, A. A.: Contact Dermatitis, Philadelphia: Lea & Febiger, 1967.
6. MacDonald, C. J.: Mycosis Fungoides; A Malignant Cutaneous Lymphoma *Conn. Med.* 32: , 1968.
7. Peterka, E. S., Lynch, F. W., and Goltz, R. W.: An association between Bowen's disease and internal cancer. *Arch. Derm.* 84: 623-629, 1961.

Mycosis Fungoides: A Malignant Cutaneous Lymphoma

Charles J. McDonald, M.D.

Introduction

Diseases of the hematopoietic system that primarily affect lymph nodes are collectively classed as malignant lymphomas. Lymphosarcoma, reticulum cell sarcoma, follicular lymphoma and Hodgkin's disease are malignant lymphomas that affect the reticuloendothelial system primarily and the skin secondarily. Excluding a small number of physicians who challenge the concept, it is generally agreed that mycosis fungoides is a malignant lymphoma that affects the skin primarily and involves visceral organs secondarily.¹⁻³ Cutaneous lesions are present at all times in untreated cases; visceral lesions occur in 40 to 50% of affected patients.⁴ Visceral lesions infrequently cause death in patients with this disease.

Mycosis fungoides is a relatively rare disease and, like most malignancies, has no known cause. It usually occurs in adults beyond 40 years of age. The clinical course may be rapid and unrelenting over a period of months, or it may be chronic and characterized by periods of remission lasting several decades. The outcome however is almost always fatal.

The appellation mycosis fungoides is descriptive and does not imply that this disease is related to the mycotic or fungus disease caused by plant parasites. The disease is so named because of the mushroom-like tumors that are often seen in late stages.

Mycosis fungoides is often very difficult to diagnose in its early stages. Because the early stages are most amenable to the various therapeutic modalities, the early diagnostic features of this disease and the salient features of several skin diseases which often precede or accompany mycosis fungoides will be discussed in detail.

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STAGES OF DISEASE: Mycosis fungoides is characterized by three clinical stages which are significant prognostically and therapeutically. They may be observed singly or in combination; either stage may be the first manifestation of disease. They are characterized by their clinical and histologic appearance.

Stage one is the eczematous or premycotic stage; it is the least malignant of the three stages; prognosis for longevity is good and therapy is often quite successful. This stage is characterized by a multiplicity of cutaneous eruptions that simulate a wide variety of dermatoses such as eczema, superficial fungus infections, psoriasis, seborrheic dermatitis, fixed drug eruptions, erythroderma and exfoliative dermatitis. There may be red, scaling, macular lesions of variable size, scattered over many regions of the body, or the patient may present with universal redness of the skin, (Indian skin, l'homme rouge), loss of hair, thick hyperkeratotic palms, or an exfoliative dermatitis. (Fig. 1). The early lesions can persist for months or years. In

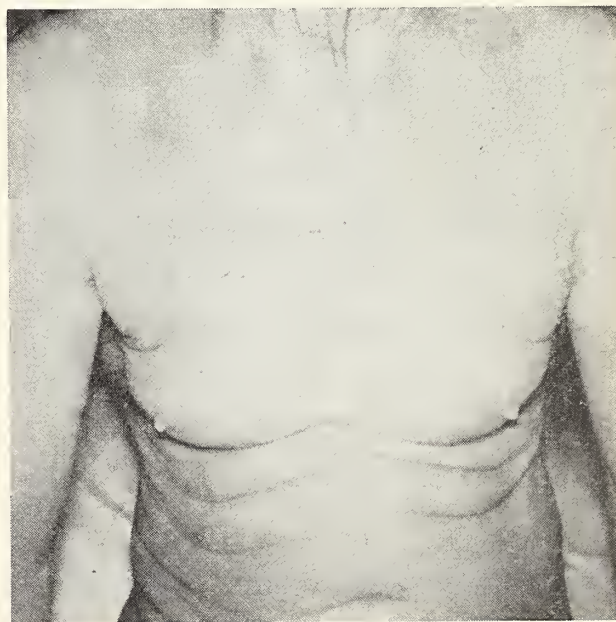


Figure 1

Erythematous and eczematous "premycotic" stage of mycosis fungoides. Note small islands of normal skin in sternal region surrounded by areas of active disease.

most cases this stage lasts 3-5 years or more; in rare cases, it may disappear spontaneously. The major symptom during this period is pruritus which is usually very intense and unrelenting. Pruritus is so characteristic of mycosis fungoides that it is well to suspect this disease in any patient over 40 years of age with an acute dermatitis and extreme pruritus.

Histologically this first stage of the disease is often difficult to diagnose and therapy may, of necessity, be instituted without a definitive diagnosis. The epidermis may be thickened and the rete ridges elongated, simulating psoriasis. Focal spongiosis, microvesiculation and inflammatory cells are noted in the epidermis. The stratum corneum is hyperkeratotic without parakeratosis. The dermal cellular infiltrate is nonspecific, consisting of loose aggregations of lymphocytes, neutrophils, eosinophils, plasma cells and histiocytes located perivascularly and throughout the dermis.^{1, 2} Occasionally in this stage, but more often in the infiltrated and tumor stages, a specific cell appears in the dermal infiltrate which suggests the diagnosis of mycosis fungoides. This cell, the so called "mycosis cell", is slightly larger than a monocyte, and is round with a large hyperchromatic nucleus and basophilic cytoplasm. Many pathologists feel that this cell is not very specific and is nothing more than a large immature reticulum cell.

In the classical progression of this disease, after a variable period of time, stage two appears. This is the infiltrated or plaque stage. Well defined, elevated plaques or nodules are seen. They vary in color from bluish red to brown, and are indurated on palpation (Fig. 2).

The histologic picture now becomes more characteristic.^{1, 2} In a compact zone in the subepidermal region there is a cellular infiltrate which is somewhat similar to that observed in Hodgkins disease. There is a multiplicity of cell types, neutrophils, lymphocytes, eosinophils, plasma cells and a polymorphism of histiocytes. A so called "Grenz zone", or cell free subepidermal region, may separate the infiltrate from the epidermis. However it is not unusual to note the infiltrate encroaching on and invading the epidermis. In the epidermis, collections of these cells form microabscesses, ("Pautrier microabscesses"), which are considered pathognomonic of mycosis fungoides.

The third and final stage, the tumor stage, develops soon after the appearance of the infiltrative-plaque stage except in the *d'embleé* type where the disease makes its initial appearance as tumors and

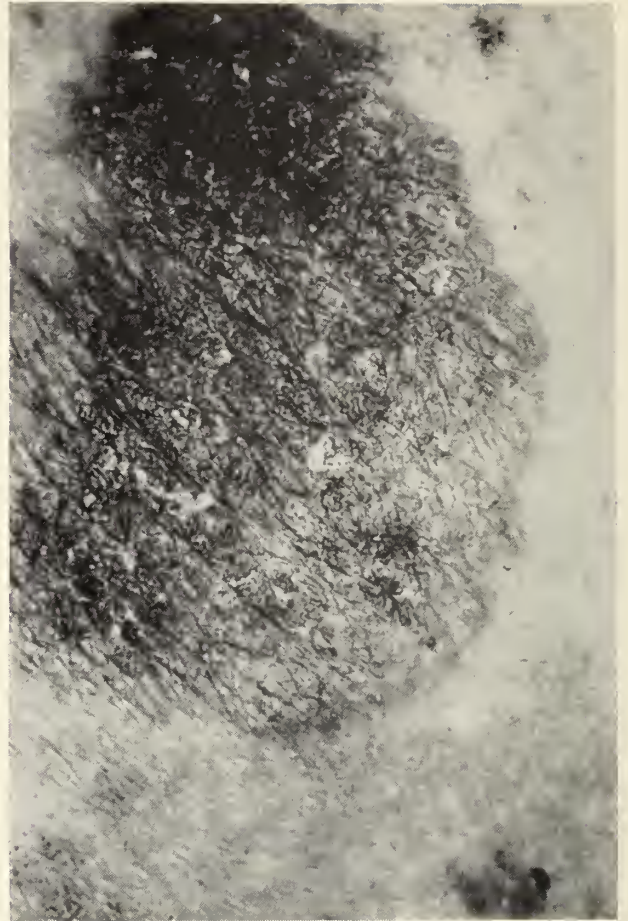


Figure 2

Plaque type lesion. Erythema, scaling and a slightly elevated border are prominent.

nodules. Tumors and nodules tend to occur in previously affected skin sites or, occasionally, in normal appearing skin. They vary in size from 1 centimeter to several inches in diameter and are elevated above normal skin (Fig. 3, 4). These lesions often break down and form deep ulcerations. Ulcerations can also appear on apparently normal skin.

Histologically it is sometimes difficult to distinguish this stage from the plaque stage except that mycosis cells are often more prominent, and encroachment of the dermal infiltrate on the epidermis is so severe that ulcerations occur.^{1, 2} Occasionally, in tumors, immature reticulum cells completely replace all other cell types, thus simulating reticulum cell sarcoma. This phenomenon may account in part for reports describing transformation of mycosis fungoides into reticulum cell sarcoma. Death occurs soon after the onset of the tumor stage. Most patients die of intercurrent infection with septicemia. A few die of visceral organ involve-

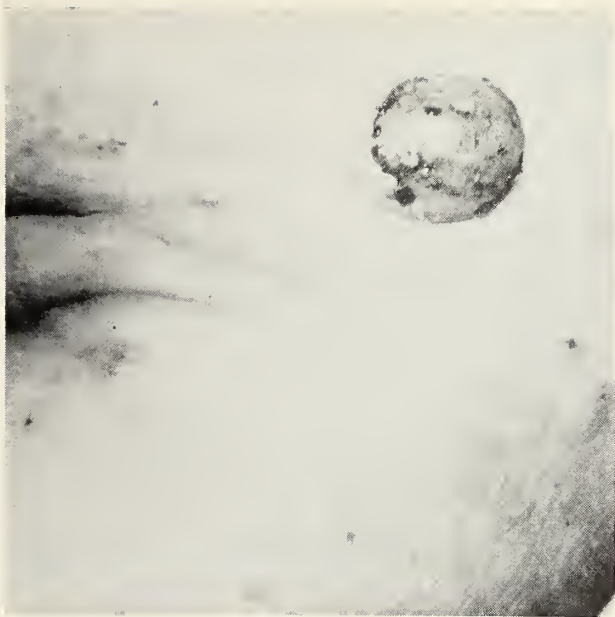


Figure 3

Large mushroom-like tumor that is characteristic of late stages of disease.



Figure 4

Large ulcerated lesion involving major portion of scalp. Disease is now approaching the terminal stage.

ment or with clinical and histologic manifestations of Hodgkins disease, reticulum cell sarcoma, lymphosarcoma, and/or leukemia.^{4, 5}

MANIFESTATIONS IN INTERNAL ORGANS: Internal organ involvement occurs in a reasonably large number of patients. Lymphadenopathy is the most common clinical manifestation of visceral involvement. The spleen, lungs, liver, kid-

neys, and gastrointestinal tract may demonstrate, on histologic examination, the specific pathologic lesion of mycosis fungoides. Those cases which do not transform into leukemia, or present as Sezary's reticulosis, show lack of obvious peripheral blood or bone marrow involvement. However, it has been observed that less than therapeutic doses of anti-neoplastic agents will produce hematopoietic suppression, in patients with mycosis fungoides as manifested by a reduction in peripheral white cell count. This does not usually occur in normal patients or in patients with other malignant lymphomas. Sezary's reticulosis, generally considered a variant of mycosis fungoides, is manifested by abnormal or 'monocytoid' cells in the peripheral blood.

On histologic examination of a lymph node, one of several changes is noted. *Dermatopathic lymphadenopathy* is more commonly observed than specific types of infiltrates. There is obliteration of the normal nodal architecture by collections of immature reticulum cells, plasma cells, eosinophils and numerous fat and melanin filled macrophages.^{1, 2} This histologic finding is often mistaken for lymphomatous node involvement, but it is characteristic of the histologic picture found associated with many inflammatory diseases of the skin which involve large body areas. Uncommonly a pathologic lymph node will resemble one of the other malignant lymphomas. In other visceral organs, small foci of abnormal cells may resemble closely the polymorphous infiltrates found in diseased skin.

CUTANEOUS LESIONS ASSOCIATED WITH MYCOSIS FUNGOIDES: There are several dermatologic diseases which, when observed in middle aged or older persons, call for investigations to rule in or out mycosis fungoides. Patients having either of these diseases and in whom there is absence of sufficient evidence to support a diagnosis of mycosis fungoides should be kept under close clinical observation for the subsequent development of this disease.

Follicular mucinosis: In 1954 Allen described mucinous changes in hair follicles in a case of mycosis fungoides.⁶ In 1957 Pinkus described a disease characterized by erythematous, scaly, eczematous, coalescent papules and plaques on several body areas including the scalp. Alopecia commonly accompanied these changes especially when lesions occurred on the scalp. He called his disorder alopecia mucinosa.⁷ Histologically this disease was characterized by mucinous changes in hair follicles. Allen believes that follicular mucinosis is a manifestation

of mycosis fungoides or other malignant lymphomas. Pinkus and others believe that follicular mucinosis occurs in benign idiopathic alopecia mucinosa and as a stage in the progression of the disease alopecia mucinosa to mycosis fungoides and other malignant lymphomas.

Parapsoriasis en plaques: Parapsoriasis is a term applied to a variety of diseases which are characterized by slowly developing, asymptomatic, scaling erythrodermas. In the *en plaque* form of the disease, well delineated patches of varying size, shape and color occur on the trunk and limbs. These patches vary in color from brown to red to purple, and are moderately scaly. They may be elevated above the surrounding normal skin. They are persistent and treatment to date is ineffective.

Many observers believe that the *en plaque* type of parapsoriasis is either a forerunner or variant of the premycotic form of mycosis fungoides. There are others who feel that the various forms of parapsoriasis never eventuate in mycosis fungoides, and those cases which have been described as such are early cases of mycosis fungoides that have been erroneously diagnosed.^{1, 8} Whether one ascribes to either belief is not important. It is extremely important to attempt to differentiate active mycosis fungoides from parapsoriasis and to maintain close observations on patients diagnosed as having parapsoriasis *en plaque* since these patients may in fact suffer with active mycosis fungoides.

Erythroderma: This is a nonspecific eruption and may occur in any of the malignant lymphomas. Erythroderma or red skin accounts for one fourth to one third of all cutaneous manifestations of lymphoma. It is usually generalized and accompanied by alopecia, loss of nails, hyperpigmentation, exfoliation, and keratoderma of the palms and soles. Pruritus is often the major symptomatic complaint. Erythroderma associated with lymphoma is usually without specific evidence of neoplastic changes in the skin, and is considered an indicator of good host resistance.⁹ When host resistance is overcome, infiltrates characteristic of the specific lymphomatous disease appear and tumors begin to develop. Pruritus usually disappears at this time.

Poikiloderma: This is a rare cutaneous condition that simulates, to a degree, radiation or solar dermatitis. Clinically it is characterized by large areas of hyperpigmentation, depigmentation, cutaneous atrophy and telangiectasia. It may appear on any area of the body and is often symmetrical. The clinical course is characterized by slowly progressive disease that is ultimately accompanied by my-

cosis fungoides, other lymphoblastomas, collagen vascular disease or cancer.

Sezary's reticulosis: Clinically and pathologically this disease is very difficult to distinguish from mycosis fungoides. Characteristically there is a generalized, erythematous, eczematous, scaling dermatitis associated with alopecia and hyperkeratosis of the palms and soles. Histologic changes in the skin are not unlike those observed in classical cases of mycosis fungoides. An abnormal "monocytoid" cell is found in the peripheral blood and is offered by some as evidence that this entity differs from mycosis fungoides which normally is not accompanied by changes in peripheral blood. Studies to refute this point of view have been reported by Fleischmajer and Eisenberg.¹⁰ Very much like mycosis fungoides, this disease is uniformly fatal.

Petechiae: Eczematous, psoriasiform, bullous, erythrodermic and other types of dermatoses have been described as preceding or accompanying the onset of mycosis fungoides. Recently we have been impressed by the presentation of several patients with a dermatologic manifestation heretofore undescribed in active mycosis fungoides. These patients have had petechiae as a major manifestation of active disease. Successful therapy has resulted in complete disappearance of petechiae, exacerbations of disease have been accompanied by recurrence of petechiae. Histologic changes in these areas are typical of those observed in mycosis fungoides.

THERAPY: The present treatment of mycosis fungoides, like that of most malignant lymphomas, is palliative. Topical corticosteroids, with or without occlusive dressings, alkylating agents such as nitrogen mustards and cytoxan, antimetabolites as methotrexate, the vinca alkaloids, vincristine and vinblastine, and antibiotics such as actinomycin D have been used as therapeutic agents with varying degrees of success. The most consistent therapeutic responses have been noted in patients treated with cytoxan and methotrexate. Therapeutic results are good in 50% of patients treated with either of these agents. They may evoke remissions that last from 3 to 6 months.¹¹ Toxic drug reactions occur in a high percentage of treated patients. Leucopenia, thrombocytopenia, nausea, vomiting, hair loss and various acute dermatoses are manifestations of drug toxicity. Refractoriness to various drugs tends to occur after repeated courses of therapy. This factor along with drug toxicity limits the usefulness of chemotherapeutic agents.

Recently two preliminary reports have appeared describing results using the antimetabolite triacetyl

6-azauridine in mycosis fungoides.^{12, 13} Seven of eight patients with stages two and three of the disease have experienced good to excellent responses with this drug. Five of the eight patients experienced complete disappearance of clinical evidence and symptoms of disease. Two patients have been in complete clinical remission for 12 and 26 months while maintained on drug therapy. Drug toxicity to date has been minimal.

Radiotherapy has been most effective form of therapy. Although no cases have been reported cured with this modality, good clinical remissions are produced in 75-85% of treated patients. Unfortunately, like chemotherapeutic agents, radiotherapy has many serious limitations, 1) as the number of courses is repeated, disease refractoryness tends to occur, 2) there is a maximum amount of radiation tolerated by the skin beyond which there is irreparable cutaneous damage, 3) there are systemic limitations to the amount of total body radiation which can be given to any one patient when using conventional X-ray techniques. This limitation has been overcome in part by using electron beam therapy as described by Fromer.¹⁴ Characteristically, electrons produced in this technique penetrate only 3 to 6 mm of skin, thus affecting areas involved with mycosis fungoides yet not penetrating deep enough to affect visceral organs. X-ray which are capable of penetrating deeper than electrons make up only a miniscule amount of the energy output of the electron apparatus and are ordinarily not productive of systemic toxicity. Like other forms of radiation therapy, there is a limit to the amount of electrons that can be administered to a single body site without evoking irreparable skin damage. The number of electron emitters in this country is very limited. Currently only five or six medical centers have such facilities available. The apparatus in use at the Yale-New Haven Medical Center is one of only three operational in the Eastern United States.

In order to take advantage of the palliative effects of radiotherapy and chemotherapy, a combined approach to the treatment of this disease is

in use at the Yale-New Haven Medical Center. For example, chemotherapeutic agents such as triacetyl 6-azauridine and methotrexate are administered in a single course sufficient to initiate a disease remission. When the disease exacerbates, the patient is given a course of electrons and chemotherapy is reinstated. This cycle is repeated indefinitely. In several patients with severe disease, this combined approach to therapy has lengthened the time between required courses of electrons. It may be assumed that in these cases this form of therapy has prolonged the patient's life and increased his comfort to a marked degree.

References

1. Allen, A. C.: *The Skin. A Clinicopathological Treatise*. 2nd ed., New York, Grune and Stratton, 1967.
2. Lever, W. F.: *Histopathology of the Skin*. 4th ed., Philadelphia, J. B. Lippincott, 1967.
3. Andrews, G. C., Domonkos, A. N.: *Diseases of the Skin*. 5th ed., Philadelphia, W. B. Saunders, 1963.
4. Block, J. B., Edgcomb, J., Eisen, A., Van Scott, E. J.: Mycosis fungoides: Natural history and aspects of its relationship to other malignant lymphomas. *Am. J. Med.*, 34:228, 1963.
5. Cyr, D. P., Geokas, M. C., Watson, G. H.: Mycosis fungoides. *A.M.A. Arch. Dermat (Chicago)*, 94:558, 1966.
6. Allen, A. C.: *The Skin. A Clinicopathological Treatise*. 1st ed., St. Louis, C. V. Mosley Co., 1954.
7. Pinkus, H.: Alopecia mucinosa. *A.M.A. Arch. Dermat.*, 76:419, 1957.
8. Ormsby, O. S., Montgomery, H. S.: *Disease of the Skin*. 8th ed., Philadelphia, Lea and Febiger, 1954.
9. Cormia, F. E., Domonkos, A. N.: Cutaneous reactions to internal malignancy. *Med. Clin. No. Am.* 49:655, 1965.
10. Fleischmajer, R., Eisenberg, S.: Sezary's reticulosis. *A.M.A. Arch. Dermat (Chicago)*, 89:9, 1964.
11. Wright, J. C.: Observations on the use of cancer chemotherapeutic agents in patients with mycosis fungoides. *Cancer* 17:1045, 1964.
12. Calabresi, P. C., Turner, R. W.: Beneficial effects of triacetyl 6-azauridine in psoriasis and mycosis fungoides. *Ann. Int. Med.* 64:352, 1966.
13. McDonald, C. J., Calabresi, P. C., DeConti, R. C.: Triacetyl 6-azauridine in mycosis fungoides. *Proceedings XIII, Int. Cong. of Dermat.* Ed. W. Jadassoh and C. G. Schirren, Springer-Verlag, Berlin, Heidelberg, New York, 739, 1967.
14. Fromer, J. L., Smedal, M. I., Trump, J. G., Wright, K. A.: High energy electrons for generalized superficial dermatoses. *A.M.A. Arch. Dermat (Chicago)*, 71:391, 1955

Telangiectasia as A Sign of Systemic Disease

Irwin M. Braverman, M.D.

Dilated blood vessels in the skin are usually considered a cosmetic problem and of no medical significance. The purpose of this paper is to outline the varieties and features of the most common types of telangiectasia and to distinguish them from the telangiectatic syndromes indicating systemic disease. If examination of the distribution and morphology of telangiectasia were performed as carefully as the observation of other types of skin lesions—for example, those considered in the diagnosis of erythema nodosum, secondary syphilis, etc., then the telangiectatic syndromes associated with systemic disease would be recognized just as easily.

Telangiectasia consists of dilated venules, capillaries or arterioles in the skin that vary in appearance from fine wires to coarse cords 0.5 mm in diameter. Although these vascular changes often can be detected without magnification, sometimes a hand lens is required.

Perhaps the most common example of telangiectasia is that found in actinically damaged skin. The affected individual is often of Anglo-Saxon origin, blue-eyed, freckled and does not tan well. Mottled hyperpigmentation and ruddiness appear on the face, "V" of the neck and chest and other exposed parts after many years of exposure to sunlight. Fine and coarse telangiectatic vessels, scattered randomly like individual twigs in the sun damaged skin contribute to the ruddy complexion.

In rosacea, broad elongated bluish venules course over the cheeks and nose on a background of erythema and pustules. The telangiectasia of rosacea is distinct from that of actinically damaged skin and resembles the facial vascular changes found in hypercorticism and polycythemia vera. In fact, polycythemia vera with facial rubror and telangiectasia is misdiagnosed as acne rosacea. Chronic flushing in the carcinoid syndrome produces identical changes.

The hallmarks of radiodermatitis are short, coarse telangiectatic vessels developing in atrophic hyper- and hypopigmented skin. Without telangiectasia, a diagnosis of radiodermatitis cannot be made.

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The spider angioma is the best known type of telangiectasia—a central pulsating punctum, often slightly elevated, with symmetrically radiating legs (Fig. 1). When the central point is compressed the legs disappear. In its earliest stage the spider is merely a tiny red spot with a pale halo. The surrounding pallor probably is due to shunting of blood from the periphery to the center because when the punctum is compressed the skin returns to its normal pink color; and when central pressure is released the ring of pallor appears as the punctum reforms. In its most highly developed state, the spider angioma looks like a strawberry hemangioma and can measure up to 2 cm in diameter as the arterioles feeding the center proliferate and produce an elevated mass. Although spiders are associated most commonly with cirrhosis and pregnancy, they occur idiopathically in children and young adults. Some patients with metastatic carcinoma to the liver may develop the cutaneous signs associated with cirrhosis including spider angiomas.

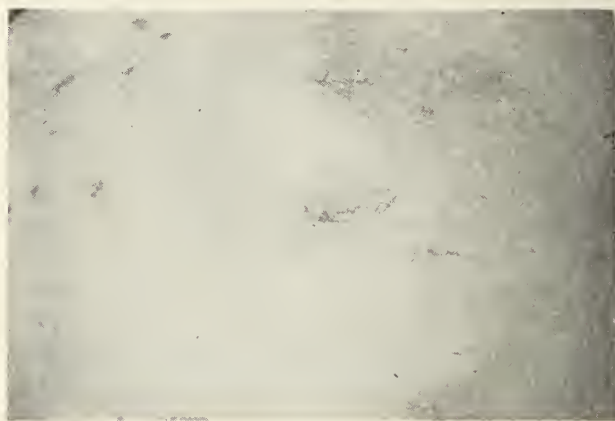


Figure 1
Spider angioma.

Specific patterns of telangiectasia develop in two-thirds of patients with connective tissue disease, and have the same diagnostic significance as the other cutaneous signs in these disorders. At times they are the only stigmata of the systemic illness.

A pathognomonic sign of connective tissue disease such as lupus erythematosus, dermatomyositis

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and scleroderma is cuticular telangiectasia (Fig. 2). Linear, wiry vessels, perpendicular to the base of the nail, appear on the posterior nailfold. They are usually bright red but appear black if thrombosed. In lupus erythematosus and dermatomyositis there is usually an associated periungual erythema, but in scleroderma the dilated vessels develop on normally colored skin. Although these dilated vessels have been studied extensively by capillary microscopy, their easy detection with the naked eye has not been sufficiently emphasized nor has their clinical significance. Cuticular telangiectasia occurs in at least two-thirds of patients with the three connective tissue diseases, in five percent of patients with rheumatoid arthritis and in an occasional patient with allergic necrotizing vasculitis. Finding such lesions in a healthy individual without evidence of an underlying disorder has occurred only twice in my experience.



Figure 2
Cuticular telangiectasia.

Large numbers of telangiectatic vessels may develop in the periungual tissue of every nail or only a few may appear on one or two nails; however, the significance is the same. This sign is particularly helpful in diagnosing a connective tissue disease in its early phase before the distinctive features of lupus erythematosus, dermatomyositis and scleroderma develop.

Palmar-digital telangiectasia is another pattern seen almost exclusively in lupus erythematosus (Fig. 3). Red to purple discrete, oval spots, sometimes raised, appear on the palms and palmar aspects of the fingers. They are distinguished from the palmar erythema of pregnancy and cirrhosis by their discreteness and extension onto the fingers including the tips. The individual lesion blanches easily. This is not common and has been described only in

lupus erythematosus. We have not seen such lesions in dermatomyositis and scleroderma.



Figure 3
Palmar-digital telangiectasia in lupus erythematosus.

Violaceous flat topped papules (Gottron's sign) develop over the dorsal interphalangeal joints in about one third of patients with dermatomyositis. The papules evolve into atrophic hypopigmented macules; and the fine wiry telangiectasia, which may have been difficult to see in the papules, becomes obvious. These early and late lesions, designated Gottron's sign, are pathognomonic of dermatomyositis.

In scleroderma, one can find two kinds of telangiectasia. The first is a pink-to-red, well marginated macule measuring up to 4 to 5 mm which occurs most commonly on the face, palms and dorsa of the hands but also can be found on the arms. The lesions—square, rectangular or polyangular—are composed of closely packed fine vessels and are present in about 50 per cent of patients with scleroderma. They may be the only cutaneous indicator of the disease. This kind of telangiectasia is extremely uncommon in lupus erythematosus and dermatomyositis.

A second variety of telangiectasia, which has recently been emphasized in scleroderma, superficially resembles the lesions of hereditary hemorrhagic telangiectasia or Rendu-Osler-Weber disease. The acronym, *CRST*, has been applied to cases of scleroderma exhibiting these spots (1). However, only the distribution of the lesions on the lips, tongue, palate, palms and nasal mucosa suggests R-O-W disease. Close inspection of the individual spots reveals well defined macules composed of discrete vessels (Fig. 4). A punctum with radiating legs, characteristic of the lesions in R-O-W disease, is not present (Fig. 5). These spots do not bleed nor is there a family history of bleeding or similar lesions.



Figure 4

Hereditary telangiectasia-like lesions in scleroderma.



Figure 5

Telangiectasia of Osler's disease.

In a few cases of scleroderma, telangiectatic spots also have been found in the gastrointestinal mucosa.

Such telangiectasia which superficially resembles that seen in R-O-W disease can be the only cutaneous sign indicative of scleroderma. We have seen several patients with extensive involvement of the gastrointestinal tract and lungs by scleroderma in whom this type of telangiectasia was the only cutaneous sign.

The development of Raynaud's phenomenon always raises the possibility of an underlying connective tissue disease. If patients with Raynaud's syndrome are examined carefully, many will be found to have either cuticular telangiectasia, polyangular red macules or hereditary telangiectasia-like lesions indicating the presence of scleroderma.

The telangiectasia of scleroderma usually arising in skin that is clinically and histologically normal, may be a clue to the pathogenesis of this disorder.

In Rendu-Osler-Weber disease, the vascular lesions develop primarily on the lips, nasal mucosa,

tongue, palms and palate but they also can be found under the nails, on the soles and even on the tympanic membrane. The true lesion of Osler's disease tends to be slightly elevated with an ill defined border and one or more legs radiating from an eccentrically placed punctum (Fig. 5). The color is usually dark red, resembling a ruby. Although some lesions in Osler's disease can be flat with sharp borders, the majority conform to the above description. Stress is placed on these fine distinctions because the lesions resembling those in Osler's disease have been observed only in scleroderma and should be distinguished from those of hereditary hemorrhagic telangiectasia.

Melena and epistaxes are the most frequent complications of R-O-W disease because of telangiectasia in the gastrointestinal tract and nasal mucosa. Arteriovenous fistulae develop in the lung and may produce coin lesions in chest radiographs. Although most patients with R-O-W disease give a positive family history, in occasional patients with the disorder the family history is negative.

Telangiectasia is also the diagnostic cutaneous sign of the Louis-Bar syndrome—ataxia-telangiectasia. This disorder appears as cerebellar ataxia in children shortly after they begin to walk. Sinopulmonary infections are frequent, immunoglobulin synthesis is impaired, and many of the patients develop malignant lymphomas if they survive into their late teens and early twenties. The diagnosis can be established at about 3 years of age when the telangiectasia appears. Fine, wiry elongated vessels course over the pinnae and bulbar conjunctivae (Fig. 6); and short stubby vessels appear in the antecubital and popliteal spaces and on the sides of the neck. Such vascular lesions also appear on the butterfly area of the face and on the palate.

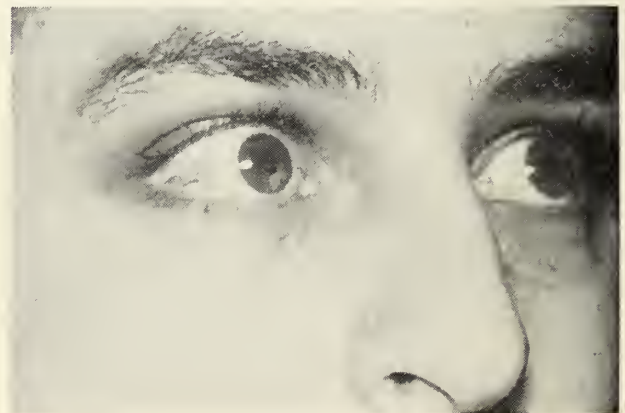


Figure 6

Scleral telangiectasia of Louis-Bar syndrome

Telangiectasia is a significant feature of the cutaneous lesions in a number of other conditions besides actinically damaged skin and radiodermatitis.

Basal cell tumors are very common and can be diagnosed early if the characteristic telangiectasis is looked for. Basal cell tumors are translucent papules or nodules that tend to expand with an elevated pearly border leaving behind a necrotic center. Many fine, wiry vessels can be found on the raised margin. In its earliest stage, when the tumor is no more than 1-2 mm in diameter, one can almost always find a wiry vessel running from the base to the apex. Such telangiectasia is not a feature of epidermoid cancer.

Degos' disease, malignant atrophic papulosis, is a very rare illness in which the vascular lumina undergo gradual obliteration. When the dermal vessels are affected, a triangular zone of homogenized collagen with an overlying atrophic epidermis results. Involvement of other organs, such as the gastrointestinal tract, brain, eye, etc. results in analogous tissue changes so that the gross appearance of the lesion is remarkably similar to that seen in the skin.

Clinically the lesions are discrete, porcelain white spots on the periphery of which are palisading wiry telangiectases. Identical lesions are found in the cerebral cortex, sclerae and gastrointestinal tract. Posttraumatic scarring does not mimic this unique lesion. The most common cause of death in Degos' disease is intestinal perforation with peritonitis secondary to the atrophic spots in the gastrointestinal tract.

Sarcoidosis and the malignant lymphomas may have red and purplish plaques and tumors with large dilated venules running over their surfaces. This telangiectasia is made up of large vessels and is strikingly different from the fine short telangiectasia found in the skin lesions of lupus erythematosus.

Poikiloderma is characterized by mottled hyper- and hypopigmentation, atrophy and fine telangiectases over large areas of the skin. It is most often found during the chronic phases of dermatomyositis and lupus erythematosus in the light exposed areas.

Poikiloderma vasculare atrophicans is a special variant in which the erythema is replaced by a red-brown color, and the lesions develop as large patches over the lower back, buttocks and thighs. It is sometimes diagnosed as parapsoriasis on plaques and is a precursor of mycosis fungoides.

Patients with xeroderma pigmentosum have an unusually rapid deterioration of their skin on exposure to sunlight with an appearance simulating generalized radiodermatitis. By 3 or 4 years of age, they have multiple skin cancers: epidermoid cancer, basal cell tumors and melanomas.

Telangiectasia is the striking feature of necrobiosis lipidica which is usually a sign of diabetes mellitus or the pre-diabetic state.

Not all widespread telangiectasia indicates systemic disease. Generalized essential telangiectasia is a spectacular but benign cutaneous entity which develops most commonly in women in the fourth and fifth decades (2). In some instances this telangiectasia is familial. The disorder begins on the legs and slowly spreads to involve the thighs, lower abdomen and occasionally the arms. Two varieties of telangiectases are present: large venous stars consisting of superficial varicosities and bright red blotchy erythema produced by many wiry vessels (Fig. 7). Although the disorder is usually slowly progressive and asymptomatic for many years, it can subside spontaneously. Regression of lesions occurs only rarely and, although this syndrome presents a serious cosmetic problem for some patients, it does not indicate systemic involvement.

Spider angiomas as well as clusters of dilated vessels can appear in a segmental distribution shortly after birth or in early childhood. They are uncommon, not associated with systemic involvement and represent a vascular birthmark.



Figure 7

Blotchy telangiectatic erythema of generalized essential telangiectasia.

The fine morphology and distribution patterns of telangiectasia are many, but careful examination allows one to separate the banal from the significant. In the process, systemic disease can be uncovered.

References

1. Winterbauer, R. H., Multiple Telangiectasia, Raynaud's Phenomenon, Sclerodactyly and Subcutaneous Calcinosis. A Syndrome Mimicking Hereditary Hemorrhagic Telangiectasia. *Bull. J. Hopkins Hosp.* 114: 361-383, 1964
2. McGrae, J. D., J., and Winkelmann, R. K. Generalized Essential Telangiectasia. *J.A.M.A.* 185: 909-913, 1963.

Places For Personal Health Care

When almost any community holds the mirror of a self-study up to its health services, it usually discovers that one place—one facility—has the center of the stage for patient care: the hospital. How the responsibility of a hospital is conceived for comprehensive personal health care, and how the hospital thus develops its services to deliver both the in-hospital and the out-of-hospital care available and accessible to all the people will determine whether or not other facilities and services will be established effectively—that is, in the home, in extended care facilities, and in more specialized centers. The community's general hospitals increasingly are broadening the scope of their activities beyond their four walls, and in so doing are more and more taking on a role in coordinating broader community health services and facilities. In fact, changing concepts and characteristics of hospital utilization are pointing to the hospital—a dynamic operation involving government board, medical staff, and administration—as a center for community health services or the locus of a community health campus.

The integration of health care agencies can be assisted by geographical proximity, each maintaining operating independence but having a more workable opportunity to cooperate for the benefit of patients and agencies. Some communities, looking to coordinating present services and filling future needs, are experimenting with the "health campus" approach. Such a campus groups certain community health care facilities and services: the official health department, offices of voluntary health associations, offices for physicians, laboratories, extended care facilities, nursing homes, rehabilitation centers, mental health centers, and, of course, the hospital. Even though geographic proximity is not always possible, nevertheless, functional coordination is imperative. This concept applies not only in urban centers, but also in rural areas, even for the physician's office. "Satellite" hospitals or medical centers are particularly suited for rural areas.

Advocates of the campus concept point to the ease with which patients can get from needed service to needed service and the ease with which physicians and allied health personnel can move from the patient in the hospital to the one in the nursing home of the rehabilitation center. Others counter with the increased difficulty the family of the patient may have in visiting him or taking over part of his care.—*Health is a Community Affair*, Report of the National Commission on Community Health Services, Cambridge, Mass: Harvard University Press, 1966, pp 101-102.

Hair Transplantation

Ronald C. Savin, M.D.

Since the beginning of medical history, baldness has been man's tonsorial enigma. Ancients such as Galen believed that baldness was due to the eating of mushrooms. In the sixteenth century, baldness was thought to be due to the loss of moisture from the scalp. Even today, hair loss has been attributed to vague causes such as the lack of shampooing, lack of brushing, or the use of a toupee.

Supposed remedies for baldness are legion. Ancient texts suggest potions made from animal sexual organs. Common treatment in Medieval times was the heavy purgation of the bowels, phlebotomy, or special diet. Acupuncture was tried but was apparently unpopular with patients. Even today unscrupulous hair specialists advertise money-back, guaranteed cures with apparent financial success.

During the past decade, three methods of surgical correction of male pattern baldness have been devised. One method is the plastic surgical technique of swinging pedicled flaps or implanting large full thickness grafts from the side of the head to the top. Though the procedure appears reasonable, there have not been signs of laudatory success. The graft tends to lose a large number of hairs due to partial necrosis. An artificial appearance is produced by the unnaturally sharp demarcation of the hair line and the elevation of the graft. The latter is caused by the thickness of the adipose layer in the posterior scalp.

Another method involved inserting nylon filaments with barbed tips into the bald scalp.¹ These nylon filaments simulated natural hair, but within a few weeks most of the nylon hairs either fell out or were rejected due to a foreign body reaction.

In 1959 Orentreich demonstrated that plugs of full thickness skin, containing multiple hair follicles, could be transplanted from the sides and back of the scalp to the bald anterior scalp of men with male pattern baldness.² After two years the hair within the grafts continued to grow normally despite further recession of "native" hair surrounding the graft. This experiment demonstrated that autographs containing the complete hair organ could be transplanted from one area of the scalp to another without modifying the natural course of

hair growth of the donor area. In male pattern baldness the fact that the hair on the side and back of the scalp continues to grow suggests that the hair organ in the posterior scalp is remarkably different from the hair organ in the crown.

Orentreich's experiment provided the groundwork for the development of the relatively simple office procedure in which the hair of the scalp can be permanently redistributed in order to gain a cosmetically acceptable pate. Thousands of patients have received this treatment over the past few years without report of serious side effects.

Technique

In male pattern baldness it is the hair on the temporal and occipital portions of the scalp which has permanence and is normally retained and which produces the characteristic horseshoe appearance. Therefore, the donor grafts must be taken from this area.

The procedure is usually performed in the physician's office. Premedication with sedatives or tranquilizers is helpful in the anxious patient. Good scalp hygiene is mandatory; the scalp should be free of dandruff or infection. It is important that the patient and the doctor should have given prior consideration to the establishment of the anterior hair line. The patient should be aware of the limitations of the procedure and the possibility of further natural hair loss. For practical reasons he should be willing to accept a sophisticated mildly receding hairline.

After proper draping, the patient reclines upon a common surgical table. Though the sitting position is initially more convenient, the patient often becomes pale, nauseated, or inclined to faint. For that reason, a supine position is best.

The anterior scalp along the recipient line is first infiltrated with 2 percent Xylocaine with epinephrine. Usually only three or four ml. are necessary to infiltrate the anterior field. Then approximately twenty 3.5 millimeter plugs are removed from the eventual recipient site. These plugs consist of full thickness skin taken with a 3.5 millimeter skin biopsy punch. The Orentreich punch has a short knurled handle devised to facilitate rotation and is most convenient to use. The plug is then elevated and the base is severed using a cataract scissors. These plugs are accumulated and

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discarded. After the plugs of skin are removed from the recipient site, the area is covered with telfa and a pressure dressing applied. The patient is then repositioned, often in a prone position, in order to facilitate the removal of the donor grafts.

The donor site in the temporal-occipital scalp is marked out with ink and the field cleansed with ethyl alcohol. The hair in this area emerges at an acute angle with the skin and, therefore, it is necessary to angle the punch so as not to sever the hair follicles. The skin is again infiltrated with 2% Xylocaine containing epinephrine. This may be done almost painlessly if a small area is first sprayed with ethylchloride. It is rarely necessary to use more than 8 mls. of Xylocaine during the entire procedure. In rapid fashion the appropriate number of incisions are made in the skin using the Orentreich punch held at the proper angle. The grafts are taken at close intervals of 2 to 5 millimeters.

The donor punches are carefully lifted and cut free of the fat, the physician being careful not to lacerate the hair follicle, and the punches are then transferred to a sterile Petri dish containing saline to prevent drying. This is extremely important as drying will result in death of the graft.

At this point an effective pressure dressing is applied to both the anterior and posterior scalp using both gauze and elastic bandage.

The donor grafts are carefully trimmed of excess fat, as well as excess hair from the exterior surface. The hair follicles sometimes protrude deeply into the fat and the utmost care is required so as not to cut off the tips of the hair bulbs. A magnifying device is useful for this purpose.

After an interval of ten or fifteen minutes the patient is returned to the operating table and the bandages removed. Hemostasis is usually adequate at this point. Occasionally bleeding is profuse from one or more sites and is stopped by the forceful application of pressure for five minutes. In cases of uncontrollable bleeding, suturing may be necessary.

The donor sites in the temporal-occipital scalp are left to heal by secondary intention. Suturing is unnecessary; because of the tension on the skin of the scalp, suturing of the donor incisions does not prevent spreading of the scars. Healing proceeds promptly from the edges of the wounds and results in small hairless scars. The eventual appearance of the posterior scalp becomes unrecognizable as the donor site, except on close examination.

When bandages have been removed, the recipient sites are filled with clotted blood. This is re-

moved easily by a rat-toothed forceps or by wiping the area with a sterile Q-tip. Bleeding often resumes but the insertion of the graft helps to achieve hemostasis. The grafts are rotated and pressed into the recipient sites until the grafts fit level with the surrounding skin and the hairs are properly orientated. It is best if the hairs are angled anteriorly along the anterior scalp and laterally as one proceeds toward the posterior scalp.

The skin from the donor site is somewhat thicker than the skin of the anterior scalp. Therefore, some plugs will protrude as much as one or two millimeters above the surrounding skin. When possible it is best to reposition the plug so that it is flush with the surrounding skin. But, if that is not possible, the plugs may be secured in place as is; during the healing process a natural reorganization of the graft will result in a smooth appearance. If it does not, the graft can be planed or shaved at a latter date.

After the plugs are inserted they will appear markedly pale compared with the surrounding skin. This is obviously due to the lack of adequate circulation.

Both smaller and larger punches may be used such as 2, 3, or 4 millimeter. These will provide relatively more or less hair. The 2 or 3 millimeter punch may be used to fill in bare areas in the anterior hair line in order to achieve a more natural appearance. The 4 millimeter punch containing a much larger number of hair follicles is useful in filling in the posterior scalp. At times it is advantageous to fit a 4 millimeter graft into a 3.5 millimeter recipient site by carefully trimming the non-hair bearing skin of the graft. This achieves a greater density of hair.

Along the anterior hair line, the grafts are placed approximately 3.5 millimeters apart. After several weeks, when complete healing has occurred, the intervening scalp may be excised and grafted so that the anterior hair line is a continuous line. I prefer to reconstruct the hair line by creating the anterior portion first and then, filling in posteriorly. The reverse order may be carried out and is desirable in the suspicious patient who may not complete transplantation. After the frontal hairline has been established, the remaining barren skin is filled in by placing the plugs approximately 3 to 5 millimeters apart.

The grafts are secured in place by Ster-strip paper tape. I prefer to cover only part of the graft to prevent occlusion. Both recipient and donor sites are then covered with telfa. A pressure dressing

consisting of two rolls of Kling surmounted by an elastic bandage is applied. This bandage has a tendency to ride up and must be secured by taping to the surrounding skin.

The pressure dressing is removed the next day and reveals the grafts covered with a small amount of clotted blood about the steri-strips. There is usually no surrounding erythema or edema. The paper strips may be removed in about seven days. Removal before this time will result in levitation of the graft. During the initial period when the grafts are fragile and covered with tape no protective bandage is necessary as long as the patient is cautious. The area may be covered conveniently with a toupee if one is available, or a hat or lock of hair may be thrown over the grafted area.

At the end of two weeks the grafts are firmly adhered and the scalp may be shampooed. At the end of three weeks the grafts are so firmly secured and healed that the patient may participate in vigorous activities such as swimming.



Figure 1A

Recipient area after three sessions of grafting one week apart. The most anterior line of grafts is three weeks old. The posterior two rows on the reader's right are two weeks old, and the posterior grafts on the reader's left are one week old and still covered with steri-strips.

The day following transplantation the donor sites in the fringe are uncovered, left to dry, and the hair is combed so as to mask the sites. It is best if the hair has been allowed to grow long because the longer hair will serve to conceal the donor sites. This area may be washed after four



Figure 1B

Same patient 4 months later.

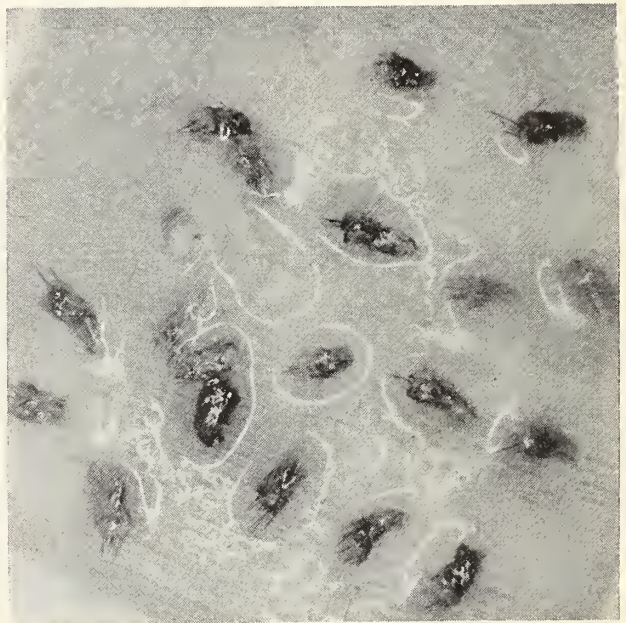


Figure 2

Full thickness grafts containing hairs.

days and no longer presents any difficulties. After three weeks careful examination will reveal numerous small, smooth, pink areas.

The hair in the grafts at the time of surgery falls out within a few weeks. This is due to the follicle reverting to the telogen phase of hair growth secondary to the trauma of the surgical procedure. After a period of at least three months, new hairs will emerge from the sites of the graft and will

grow at the normal rate of about five inches per year. Therefore, even though the transplants are rapidly carried out (though it is never rapid enough for the patient) it is at least six months before significant growth can be seen and usually twelve months before it is cosmetically satisfactory.



Figure 3A

A patient with Male Pattern Baldness during the third month of transplantation.

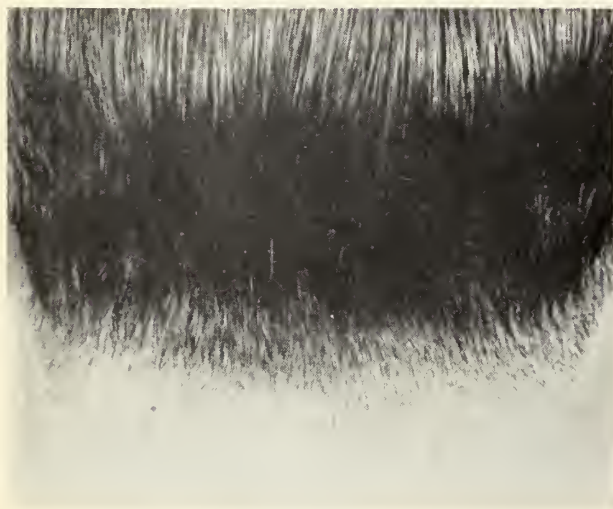


Figure 3B

Same patient fourteen months after beginning transplantation and 550 autografts.

Grafting may be carried out several times a week, but the once a week rate proves to be most convenient. This allows the operator to select different areas of the scalp at each session and for the donor area to heal before he returns to it. Fifteen to thirty plugs may be transplanted conveniently at one time. Transplanting more than forty plugs at one sitting proves to be a chore, both for the phy-



Figure 3C

Part of the donor area after 550 autografts have been removed. (Courtesy D. Bluford Stough, III, M.D., Hot Springs, Arkansas.)

sician and the patient. With too frequent sessions and large numbers of grafts, it is possible to interrupt and compromise the circulation within the skin of the scalp. At its worst this means that a few grafts may not take. This is not usually a problem as the unproductive area can be excised and subsequently re-grafted.

Discussion

Hair transplantation is not a panacea for the bald man, but rather it is a way of achieving cosmetically satisfactory redistribution of the hair in the well-motivated patient. Patients with a mildly receding hair line will require from 40 to 80 grafts. In the balding man often 200 grafts are required; and in the severely affected patient as many as 350 to 600 grafts can be inserted. Of course, the limiting factors involve the distribution density of the hair, as well as the extent of the donor site. Even in the patient with severe male pattern baldness and a narrow fringe area, 200 grafts can easily be removed from the fringe area. But in such cases, it would be more feasible to combine hair transplantation anteriorly with the use of a posterior hair piece called a divot.

Hair transplantation does not produce lush thick hair. Rather it produces a hair bearing scalp with a "youthful" hairline. The bald appearance is effectively removed. The hair is real. It may be combed, pulled, washed and grows forever in the same manner as the hair of the donor area.

Hair transplants are also quite useful in other causes of localized hair loss. In traumatic alopecia due to scarring caused by accidents or burns hair,

transplantation becomes a very effective technique in both men and women. Transplantation is usually successful within small scars or along the borders of large scars. Within the center of large burn scars the grafts are often unsuccessful because of the lack of adequate circulation.

Though alopecia areata often results in small localized areas of hair loss, transplantation is not indicated. Intra-dermal injection with steroids usually achieves excellent regrowth within a few weeks.

Modern scientific medicine has destroyed and invalidated the folk lore remedies and age old misconceptions involving male pattern baldness. Unfortunately, modern medicine has not uncovered

the seemingly simple and reasonable topical, hormonal therapy. Until it does, hair transplantation is a reasonably effective technique for redistribution of the hair of the scalp.

Though it is easy to scorn the need for hair transplantation, the psychological advantage to those enjoying a well adorned scalp is best appreciated by the disadvantaged.

References

1. Ayres, Samuel, III, M.D.: Conservative Surgical Management of Male Pattern Baldness, Arch Derm 90:492-499, 1964.
2. Orentreich, N.: Autographs in Alopecias and Other Selected Dermatological Conditions, Ann NY Acad Sci 83:463-479, (Nov. 20) 1959.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

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Skin Color: Fact and Fancy

Sidney N. Klaus, M.D.

Skin Color: Fact and Fancy

Of the many criteria which have been established to indicate racial origin, skin color is at once the most conspicuous and most popular. Unfortunately, many current notions concerning the nature and origin of skin pigmentation have been derived from myths and folktales, and, judging from recent articles in the lay press, the biologic facts related to color and race are not widely known. The purpose of this paper is to examine some common misconceptions regarding racial pigmentation and to review briefly the biologic events surrounding the pigment process.

Man has indicated an awareness of differences in skin color since the beginning of recorded history. Archaeologists have uncovered wall paintings in Egyptian tombs showing figures painted with red, yellow, black and white pigments. These figures have been interpreted as representing the Egyptians themselves and their neighbors from the East, South and North respectively.

A legend from ancient India describes an invading force from a neighboring region whose members had "black skin and flat noses." And in the Babylonian Talmud dark-skinned peoples were considered to be the descendant of Ham, a "curse of darkness" being imposed upon his progeny because he showed disrespect for his father, Noah, (Genesis 9:29).

In the Middle Ages Paracelsus argued that the people of Europe were created from a stock entirely separate from the Africans and others, who at that time were thought to occupy the rest of the earth. "God could not endure to have the rest of the world empty and so by his admirable wisdom filled the world with other men."

The first "modern" approach to racial identification was made by Blumenbach in 1775. He divided mankind into five groups on the basis of a variety of physical characteristics including skin color: Mongolians (yellow), Ethiopians (black), Americans (red), Malaysians (brown) and Caucasians (white). The 19th century biologist, Huxley devised a more broad classification in 1870. He separated the peoples of Europe into two races, the

Xanthachroid and the Melanochroids. Other 19th century anthropologists suggested more detailed schemes for classification, in some cases involving more than 30 categories of pigment shades. Today, physical anthropologists generally agree that skin color is an entirely inadequate method for determining racial identity. Not only is color difficult to measure accurately, but often there is much overlap both within and between racial groups.

Traditionally, in the designation of racial groups, the overlap was ignored, and the extremes of the spectrum were emphasized, giving rise to a number of simplistic but inaccurate labels such as BLACK POWER and WASP.

The Biology Of Skin Color

The pigments in human skin which contribute to skin color include melanin, reduced and oxidized hemoglobin, and carotene. Melanin is by far the most important pigment in the determination of skin color; and, quantitatively, it is the most variable. It should be emphasized, however, that qualitatively melanin is the same in all the races of man.

Melanin is found in human skin within the epidermis. It is produced by specific cells, melanocytes, which originate from the epithelium of the neural crest and migrate in the embryo to take up positions at the dermal-epidermal junction. All adults, regardless of skin color, have approximately the same number of melanocytes, about 2 billion. Differences in color are related to the amount of pigment produced by the melanocytes.

Melanin is formed by the action of the enzyme tyrosinase on the amino acid tyrosine. The synthesis of melanin is confined to small, oval shaped organelles, called premelanosomes, scattered throughout the cytoplasm of the melanocytes. As the tyrosinase reaction proceeds the pigment is deposited upon a membranous framework within the premelanosomes to form melanosomes (or melanin granules). Once the organelles are fully melanized, tyrosinase activity can no longer be identified within them. After the melanin granules have been formed, they are transferred to surrounding epidermal cells by direct inoculation.

The transfer process has been observed in detail in cell cultures of skin. At the beginning of the transfer process the tip of a dendrite from the pig-

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ment cell (usually containing 30-50 melanin granules) is introduced into the epidermal cell, and the tip of the dendrite is then pinched off. As the melanin granules are incorporated into the cytoplasm of the epidermal cell, the dendrite withdraws. It has been postulated that the rate of pigment transfer may control, to some degree at least, the rate of melanin synthesis within the melanocyte.

The inheritance of skin color in man is determined by at least six genes. Although the exact nature of the genetic control is not fully known, a number of agents present in human skin have been identified as inhibitors of the melanin synthesizing process. One inhibitor, reduced glutathione, has been identified recently in greater amounts in white skin than in Negro skin. The enzyme reaction that regulates the formation of reduced glutathione may be a critical one in the inherited control of skin color.

Some attempts have been made to artificially alter skin color through the use of hormones and certain topically applied drugs; however, at the present time no effective method is available.

The Origin Of Skin Color Differences

Early man not only recognized color differences, he also sought to explain their origin. The ancient Greeks attributed the variations in skin color to a natural catastrophe. They believed that Phaethon, the son of the god Helios, took the reins of the sun chariot from his father. The younger man could not control the course of the sun, however; and in some regions it passed too close to the earth, burning the people black. In others it rose too high causing the people to turn pale from the cold. According to a North American Indian legend about skin color, the creator, in baking the first man, cooked him too long, and he emerged black; the second was not baked long enough, and he remained white. It was only in the third attempt that the properly golden-brown Indian was produced.

Blumenbach gave a slightly more accurate "scientific" explanation for the origin of dark-skinned people: he thought that carbon became embedded in skin of Negroes in warm tropical climates.

Today, a number of theories about the origin of the pigmentary differences in man have been developed which are consistent with known facts, but the theories themselves are not easily tested. The

anthropologist, Coon, suggested that races of man evolved from more primitive states at varying times in history and that skin color was the result of genetic chance rather than of adaptation. Most other scientists believe that man evolved as a single race—whether he was originally light-skinned or dark-skinned is not known—and he then evolved to form the racial groups as we know them today.

The exact relationship of skin color to adaptive factors is debated. Some feel that dark pigmentation was a beneficial trait in areas of intense sunlight because of its ability to block the absorption by the deeper tissues of short ultraviolet radiation. Melanin is known to protect against disabling sunburn and the cumulative effects of radiation which often result in the development of skin cancers and melanomas. However, other workers have argued that the protective property of melanin is unimportant in adaptation and that the presence or absence of skin cancer does not significantly influence survival.

Blum has indicated that one disadvantage of dark skin in tropical areas is an increased heat load. Heer demonstrated that Negro skin absorbs 34% more energy than white.

Loomis suggested that racial distribution has been affected by the varying capacity of skins of different colors to produce Vitamin D. He has argued that because Vitamin D occurs in virtually no natural foods, primitive man had to rely to a large extent upon the radiation-induced synthesis of this vitamin to allay rickets. He has suggested that lighter skin in areas north of the 40th parallel evolved in response to Vitamin D deficiency, and the heavily pigmented skin in tropical areas served to protect against excessive Vitamin D formation.

Blum concluded that the selective pressures exerted by sunlight may best be reckoned in terms of the summation of the known effects which could conceivably lead to genetic modification. "Without more information than is available the pressure of any one of them cannot be fairly evaluated."

At the present time, dermatologists, and biologists are continuing to investigate the many puzzling facets of the pigmentation process in man. Perhaps the data they accumulate eventually will supplant the legends and help minimize prejudicial attitudes to which the folktales are often bound.

IN MEMORIAM—MAX CAPLAN, M.D.

A resolution expressing sorrow at the sudden passing of Max Caplan, M.D. Meriden, AMA Delegate and CSMS President-elect, on December 6, 1968, was unanimously adopted by the House of Delegates at the 1968 Semi-Annual Meeting on December 11 at the Stratford Motor Inn. Copies of the resolution and notice of the House action were sent to his widow and the members of his immediate family.

WHEREAS: Max Caplan, Meriden, has had a long and distinguished career as a practitioner of medicine; and

WHEREAS: Through his outstanding professional and civic endeavors, he has served well the people of his community and his state; and

WHEREAS: He has contributed unstintingly of his time and energies to the betterment of medical practice and the public health as an actively participating member and officer of the New Haven County Medical Association and the Connecticut State Medical Society, and as a Delegate to the American Medical Association; therefore be it

RESOLVED: That the members of the House of Delegates of the Connecticut State Medical Society, in meeting assembled at Stratford, Connecticut, on the 11th day of December, 1968, note with sorrow the recent passing of a distinguished colleague and valued friend, Dr. Max Caplan of Meriden, and honor his memory by observing a period of silent prayer; and be it further

RESOLVED: That this expression of tribute and respect to Dr. Caplan by the members of the House of Delegates be recorded in the minutes of this meeting, and notice thereof be transmitted to his widow and the members of his immediate family.

FROM THE GENERAL MANAGER'S OFFICE

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SUMMARY OF ACTIONS COUNCIL MEETINGS

Wednesday, November 13, 1968

Thursday, November 21, 1968

Foreword

Since only about one-half of the items on the agenda for the meeting of November 13th were completed at that meeting, and the remaining items were held over until November 21st, the minutes of the two meetings, while recorded separately, are combined for purposes of maintaining continuity.

MEETING OF NOVEMBER 13, 1968

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Caplan, Grendon, Brandon, Abbot, Fabro, Bradley, Rogol, Cramer, Egan, Petrie, Spitz, J. M. Grant, Nemoitin, Johnson, McDonald, R. F. Grant, Granoff and Wilson.

Also present were: Mrs. Lindquist, Mr. Villano, Dr. Redlich, Dr. Patterson, Dr. Hess, Dr. Ronald Beckett, Mr. Walter Lyons, Dr. E. Stuart McCleary and Dr. Richards.

Absent were: Drs. Farrell, Purnell, Shepard, Friedberg, Pelz, Palomba and Roch.

II. Routine Business

Life Membership

It was VOTED to approve an application for Life Membership received from the following eligible Active Member:

E. H. Wray, Jr., Litchfield (LCMA)—1969

Election of Student Members

It was VOTED to elect to Student Membership fifteen residents of Connecticut who are enrolled in medical schools in the United States. A list of those elected will be published in the Journal.

Date of Next Meeting

The Chairman selected Thursday, November 21, 1968, as the date for the next meeting.

III. Old, New and Special Business

Report—Committee on Hospitals

It was VOTED to accept, as information, a report filed by this Committee, and to act separately on its several sections as follows: (AMB 11/13/68 "A")

- (a) *Protection Against Suit of Physicians Serving on Utilization Review Committees:* Although the report concluded that, between their own professional liability insurance and the "blanket" liability policies carried by most hospitals, physicians already have sufficient protection in this regard, it was VOTED to direct the Committee on State Legislation to prepare a bill for the 1969 General Assembly which would grant immunity against civil suit to physicians serving on hospital utilization review committees without compensation.
- (b) *Development of Minor Surgical Facilities:* The Committee reported that the development of facilities to accommodate short-stay minor surgical patients as an aid to relieving hospital bed shortages, as proposed by a New Haven County member, presented many problems to be met and that the Committee would find it "difficult to endorse" the development of such facilities in Connecticut. The Council VOTED to refer this question back to the Committee with the request that further study be given to it with the objective of "being innovative" with respect to how such facilities might be developed and function.
- (c) *Increasing the Number of Voting Physician Members on Hospital Governing Boards:* The Committee reported that "almost unanimously (it) favored having an elected representative of the staff serve as a voting member of the governing body of the hospital." The Council VOTED to request the Committee to investigate the extent to which favored policy is being carried out in Connecticut and to make a specific recommendation to the Council as to how it could be more fully and more meaningfully implemented in hospitals throughout the state.

Report—Ad Hoc Committee on Medical Quackery re Chiropractic

As requested by the Council, Max Caplan, Meriden, Chairman of the Ad Hoc Committee (of one) on Medical Quackery, filed a comprehensive report on "A Study of the Problems Posed by Chiropractors in Connecticut, Past and Present." It was

VOTED to accept Dr. Caplan's report as information, and with commendation, and it was further VOTED to request the Ad Hoc Committee to seek co-sponsorship from the groups listed in Recommendation No. 8 in the report with a view toward planning and holding a Connecticut Conference on Chiropractic which would be open to the public.

It was also VOTED to send copies of this report to all members of Federal "Expert Review Panel on Chiropractic, Naturopathy and Aprapathy," along with copies of the AMA and CSMS positions re chiropractic, and urge the Panel to make recommendations to its appointing agency accordingly.

Finally, it was VOTED to refer to the Judicial Committee, for study and ethical ruling, the related questions of a physician accepting a patient referred to him by a chiropractor and his relationship to a chiropractor as a consultant to a patient under a chiropractor's care.

Proposed Training Program for I.V. Technicians

By invitation, Ronald S. Beckett, Hartford, and Mr. Walter Lyons, Director of Employment Development, Hartford Hospital, joined the Council to present details of a proposed training program for intravenous therapy technicians. A two-year course would provide one year of largely academic instruction in medical subjects pertinent to the technical duties contemplated, and a second year of supervised internship or "on-the-job training." Following extended discussion, it was VOTED to approve the proposed training program for I.V. technicians, as presented by Dr. Beckett and Mr. Lyons, provided that adequate training be given in all hazards relating to intravenous therapy and the prompt recognition of untoward and toxic symptoms indicative of same.

Report—Ad Hoc Committee on Annual Meeting Arrangements

It was VOTED to receive as information the report of this Ad Hoc Committee which described the format for the 1969 Annual Meeting of the Society which had been developed after consultation with members of the Committee on Program of the Scientific Assembly and representatives of most of the CSMS Sections and allied groups. In brief, the format calls for the House of Delegates to meet and complete its business in two sessions, one in the forenoon of Tuesday (the first day) and the second in the forenoon of Wednesday, the day following. The afternoons of those days, plus a full day on Thursday (the third day) have been allocated to the scientific session and Section meetings.

Pursuant to the subject of annual meeting arrangements, it was VOTED to approve the dates of May 12-13-14 for the 1970 meeting at the Hartford Hilton Hotel, Hartford.

Report—Revised Model Provisions for Medical Staff Bylaws

It was VOTED to accept, as amended, a report of the (temporarily continued) Committee on Preliminary Study of Censorship Questions, titled: "Suggested Provisions for a Model or Guide for Medical Staff Bylaws re Rules and Regulations Concerning Privileges". It was further VOTED to send copies of the report, as accepted, to the chiefs of staff of all Connecticut hospitals, to the presidents of all hospital governing boards in the state, and to the Joint Commission on Accreditation of Hospitals.

Connecticut Regional Medical Program

(a) Report of CSMS-CRMP Liaison Committee:

It was VOTED to receive as information only the report of the CSMS liaison representatives who had joined the CRMP Executive Committee in a series of meetings to attempt to resolve and/or accommodate divergent opinions on the CRMP Operating Grant Request held by the two organizations. While most members of the Council appeared to agree that considerable progress had been made, based on verbal assurances, toward accommodating most of the substantive differences as to specific programs, their content, methodology, applicability, etc., it was accepted as fact that no accommodation whatever had been achieved on the Council's insistence that there be greater representation of privately practicing physicians on the CRMP Advisory Board and Executive Committee; i.e., that, on November 13th, the CRMP Advisory Board had voted to continue to limit the number of private practitioners designated by CSMS to four on the Board and one on the Executive Committee. Pursuant to full discussion of this report and related information, in which Drs. Redlich, Patterson and Hess were invited to participate, the Council VOTED to direct that a "Revised Statement on the CRMP Operating Grant" be prepared for presentation at the RMP Site Inspection Team visit to New Haven on November 18, 1968, and for transmittal to the RMP National Advisory Council which will reconsider the CRMP Operating Grant Request the week following. The statement concludes with a resolution, adopted by the Council, which reaffirms the Council's position regarding the number of

practicing physicians that should be on the CRMP Advisory Board and Executive Committee and states the finding of the Council that, until such representation is authorized, its full approval cannot be given to the CRMP Operating Grant Request, however else revised.

MEETING OF NOVEMBER 21, 1968

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Caplan, Grendon, Brandon, Abbot, Fabro, Bradley, Cramer, Farrell, Egan, Shepard, Johnson, R. F. Grant, Pelz, Granoff, Rem (substitute Councilor from FCMA) and Roch.

Also present were: Mrs. Lindquist, Dr. Hess, Mr. Donelan (AMA) and Dr. Richards.

Absent were: Drs. Gardner, Weber, Jr., Rogol, Petrie, Spitz, Purnell, J. M. Grant, Nemoitin, Friedberg, McDonald, Wilson and Palomba; also, Drs. Redlich and Patterson, invited guests.

II. Routine Business

Life Membership

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

James J. Costanzo, Stamford (FCMA)—1968

M. T. Sheehan, Wallingford (NHCMA)—1969

Date of Next Meeting

The date for the next meeting of the Council was tentatively set for Wednesday, January 15, 1969.

III. Old, New and Special Business

Report—Committee on Public Health

(a) *On Out-of-State Laboratory Survey:* It was VOTED to receive as information a report of this Committee which summarized the results obtained from a survey of the membership as to the extent to which out-of-state laboratories' services are used by Connecticut physicians. It may be concluded, in brief, that about four physicians in ten do use such services, and that some twenty-eight such laboratories are patronized.

(b) *On Comprehensive Health Planning:* It was VOTED to accept a recommendation of the Committee that the Society seek to participate actively in Comprehensive Health Planning at the state level; urge the county medical associations to do likewise at the county level; and attempt to keep the membership well informed as to developments in such planning.

It was further VOTED to urge each county medical association and local medical society to seek to arrange for its members to become

actively involved in health planning at the community level, and to communicate directly with Commissioner Foote and the Chairman of the Advisory Council of CHP toward that end; also, that the General Manager forward to Commissioner Foote et al a list of all county associations and local medical societies, including the names and addresses of the current officers of same, so that lines of communication in both directions may be encouraged to operate.

Report—Committee on Rural Health

It was VOTED to receive as information a report of this Committee, and a follow-up communication received from its chairman, G. S. Guderhatch, recommending that the Society seek to assure the participation of "rural people (physicians and others)" in Comprehensive Health Planning activities at all levels, and it was further VOTED to adopt a resolution on this subject submitted by the Committee. Copies of the resolution will be sent to Commissioner Foote and the Chairman of the CHP Advisory Council for their consideration and response.

Joint Statement on Dependent Nursing Functions

It was VOTED to approve a statement on "Dependent Nursing Functions" which had been prepared jointly by representatives of CSMS, the Connecticut Nurses' Association and the Connecticut Hospital Association. It is expected that the governing bodies of CNA and CHA will give similar approval to the statement. In brief, the purpose of this document (if endorsed jointly) is to provide professional, administrative and moral backing to the Registered Nurse who carries out *medical* functions in hospitals, under the supervision and/or direction of staff physicians, and to place responsibility for adequately training such Registered Nurses to discharge these functions competently on the medical staff, the hospital administration and the nursing administration jointly. The objective of this program is not to authorize R.N.'s to practice medicine, but to enable them to participate fully in the modern "team" approach to patient care under carefully controlled conditions.

Re Resuming Relations with Connecticut Medical Service, Inc.

The Council was informed that the Fairfield County, Windham County, Middlesex County and possibly other component Associations, had adopted resolutions at their recent semi-annual meetings which urged the Council to explore the possibility of establishing "meaningful" or "improved" relations with CMS, Inc. In addition, the Council

received a formal communication from Dr. Bruce Thayer, Jr., Medical Director of CMS, advising the Council that the Board of Directors of CMS, Inc. had voted to invite representatives of the Society to meet with representatives appointed by the Board "to discuss areas of mutual interest and concern which could serve as an initial step in promoting a constructive and cordial relationship". It was VOTED to accept this invitation of the CMS Board, and to direct the President to form a committee of CSMS officers to meet with the Board's representatives for the purposes stipulated by the Board.

Resignations and Appointments

It was VOTED to accept with regret, and thanks for past service, the resignation of William J. Watson, New Britain, as Chairman of the Conference Committee with the Connecticut Bar Association. Dr. Watson is asked to remain on the Committee as a member. It was further VOTED to appoint J. Alfred Fabro, Torrington, a member of the Committee, to replace Dr. Watson as Chairman for the balance of the current elective year (May, 1969).

Renewal of General Manager's Contract

Having received "at least six months' written notice" that the General Manager desires to renew his agreement (contract) with the Society, the Council VOTED to approve the renewal of this agreement for another five-year term, effective May 14, 1969, when the present agreement expires. The General Manager expressed thanks to the Council members for this manifestation of their continuing confidence in him and their apparent satisfaction with his services during the past decade.

Changes in Staff Titles

It was VOTED to approve a staff suggestion that Mrs. Lindquist's title be changed from "Assistant to the General Manager" to "Associate General Manager", effective as of this meeting. It was further VOTED to approve a staff suggestion that a change be made in Dr. Richards' title from "General Manager" to "Executive Director", and that the Subcommittee to Study and Revise the Bylaws be requested to prepare an amendment to the Bylaws to accomplish that end for transmittal to the House of Delegates on December 11, 1968. It is understood that when such amendment has been approved by the House of Delegates, Mrs. Lindquist's title will change automatically to "Associate Executive Director", and it was further VOTED to request the Subcommittee to Study and Revise the Bylaws to study and report on the desirability of

listing the office of Associate Executive Director in the Bylaws.

CRMP

It was VOTED to receive as information the report of the CSMS representatives who had testified at the hearing held by the RMP Site Inspection Team in New Haven, October 18, 1968, and had formally presented Council's "Revised Statement on CRMP Operating Grant Request" to the Site Inspectors. In brief, the report stated that the Site Inspectors had commended the Council on the constructive contributions it had made to CRMP planning via the "critique" it had filed with the RMP National Advisory Council in August, and had expressed personal sympathy with the Council's position regarding substantially greater representation of privately practicing physicians within the CRMP structure at the policy-making level. However, the CSMS spokesmen had not been given any assurance that this position would be accommodated, either nationally or locally, and felt that a resolution of the matter which would be favorable to the Council might well not be forthcoming. The RMP National Advisory Council is to meet on November 25-26, 1968, at which time the CRMP Operating Grant Request will be reconsidered.

Pursuant to a lengthy discussion of this report, the Council VOTED to adopt the following motion:

IT IS MOVED: That, having heard a report on the proceedings of the RMP Site Inspection Team visit to New Haven, the Council direct that a further statement be prepared and transmitted to the RMP National Advisory Council, citing that:

- a. From the Council's standpoint, "all cooperative arrangements on which effective program implementation depend" have *not* been satisfactorily established in Connecticut.
- b. Full cooperation by physicians throughout the State is essential to the success of CRMP, and such cooperation can best be assured by having substantial representation of practicing physicians on the CRMP Advisory Board and Executive Committee (as proposed by the CSMS Council).

- c. Without such representation, the Council believes it will be difficult to mobilize maximum physician participation in CRMP operating programs.
- d. The Council is convinced that such representation is vital to assuring that the people of Connecticut will receive the greatest possible benefits from their regional Medical Program.

and that, for the foregoing reasons and others, the CSMS Council urge the RMP National Advisory Council to approve a grant request to CRMP only if approval is accompanied by a recommendation that the number of privately practicing physicians on the CRMP Advisory Board and Executive Committee be increased substantially above the present limits.

In a further action, it was VOTED to adopt another motion as follows:

IT IS MOVED: That the President appoint an Ad Hoc Committee on CRMP which would include himself, as chairman, the four representatives of the Council that are on the CRMP Advisory Board and such members of the Society who are deemed experienced in CRMP with the charge that the Ad Hoc Committee coordinate activities of the Society in relation to CRMP and, particularly, that they develop positive plans for improving medical care in Connecticut that might be submitted to CRMP for implementation.

Directive to Liaison Committee to CG on Medicare B

It was VOTED to direct the Liaison Committee with Connecticut General on Medicare B to gather as much information from all sources available to it as is possible regarding the fee levels (usual, customary, prevailing or whatever) currently being "allowed" for payment by CG on Medicare B claims, and to report to the Council whether or not there has been a change in CG's policies regarding such payments as compared with the in-

ception of Medicare B in 1966. It was further VOTED to request the Committee to seek to determine what experience has been in other states with regard to payments under the "usual, customary and reasonable charge" method.

N.B.: The foregoing is a summary of the proceedings and actions of the Council on November 13 and November 21, 1968. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.

Placement Wanted

OTOLARYNGOLOGIST—Board eligible, will finish residency June 30. Military obligations complete, desires practice opportunity.

INTERNIST—subspecialty in Infectious Diseases, recently completed residency, desires association or group practice.

NEUROLOGIST & PSYCHIATRIST—Board certified in both specialties, desires association with individual or group in Eastern Connecticut.

OBS-GYN—Board eligible, military obligations completed, wishes associate practice starting July, 1969. 30 years of age, married and has National Boards.

SURGEON—38 years old, Board certified, Connecticut license. Presently in service, but wishes to terminate active duty because of administrative work increase and desires to be in direct care of patients. Available immediately.

PEDIATRICIAN—32 years of age, military obligations completed, Board eligible. Would like to join one or more pediatricians in any area in Connecticut. Available April 1, 1969.

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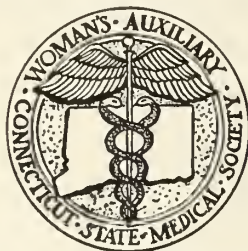
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Many of the articles in CONNECTICUT MEDICINE over the past months have been concerned with national aims and programs. It is time we looked directly at Connecticut to see what the auxiliary members have been doing. The county is the place to assess the accomplishments, and as each county is different in size and composition, the talent and competence of the women is shown in the variety of efforts. Only one or two of the special programs already run or to be done will be mentioned for each county.

Hartford County has chosen "Fiddler on the Roof" as their project to raise money for the Memorial Scholarship Fund.

A Litchfield County member, past county and state president, Mrs. Winfield Wight, was honored last spring by the Red Cross for her 10 years of dedicated service to the Bloodmobile Program in Thomaston.

Middlesex County presented a delightful International Culinary Buffet Luncheon to benefit the Health Careers Scholarship Fund. Gourmet dishes from foreign lands were prepared by auxiliary members from cherished recipes. This was received with such enthusiasm that it will likely become an annual affair.

"Job Fair for Health Careers" highlighted a successful health careers effort to inform persons interested in occupations in the health field. The Job Fair, co-sponsored by the Woman's Auxiliary to the New Haven County Medical Association and the Third Wednesday at the YW Committee, attracted many people Wednesday, October 16, to the Waterbury YWCA.

Area girls, women and men from 18 to 65 years of age were invited to attend the Job Fair and to learn about the more than 200 positions in health careers in the Waterbury area. Opportunities for health jobs are available for high school graduates,

those who have not completed high school, persons with or without college degrees, the physically handicapped and the emotionally disturbed. Physicians' wives served as Spanish and Italian interpreters.

Many persons, expert in different health fields, were available for consultation throughout the morning. Brochures and booklets explaining the needs in the various fields were distributed. It was reported that there was great interest and enthusiasm among both those participating in the program and those attending the Job Fair.

New London County's membership tea for over 40 new and prospective members was most successful. AMA-ERF will benefit from a cocktail party honoring the new area physicians and their wives in December.

Windham County continues its work with the pre-school visual screening program and its annual AMA-ERF luncheon bridge.

Each county has, in addition to the specials mentioned above, projects in other phases of auxiliary work. A complete study will be presented in the President's Annual Report later in the year.

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MEETINGS

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospitals Auditorium,
New London

February 18 7:15 P.M.

Fiberoptic Esophagoscopy and Gastroscopy

Americo Abbruzzese, M.D., Clinical Associate in
Medicine, Harvard Medical School

February 25 7:15 P.M.

Myocardial Circulation

Richard H. Gorlin, M.D., Senior in Medicine and
Director of Cardiovascular Research, Peter Bent
Brigham Hospital

CANCER

Oncology

Sponsored by the Connecticut Division of the
American Cancer Society and the Yale School of
Medicine.

Speakers: Yale School of Medicine

Russ Home Conference Room, Griffin Hospital,
Derby

February 4 8:00 A.M.-9:00 A.M.

Radiotherapy in Initial Tumor Management

Carl VonEssen, M.D., Assistant Professor of Radi-
ology

February 11 8:00 A.M.-9:00 A.M.

Radiotherapy in Control of Metastatic Disease

John Mallams, M.D., Professor of Clinical Radi-
ology

March 4 8:00 A.M.-9:00 A.M.

Tumors that Secrete Vasoactive Amines

Robert Levine, M.D., Assistant Professor of Medi-
cine and Pharmacology

March 11 8:00 A.M.-9:00 A.M.

Dermatologic Manifestations of Malignancy

Irwin Braverman, M.D., Associate Professor of
Dermatology

April 1 8:00 A.M.-9:00 A.M.

Management of Patients with Lymphoma

Ronald DeConti, M.D., Assistant Professor of Medi-
cine and Pharmacology

Chairman: Doctor DeConti; Co-Ordinator, Vincent
A. DeLuca Jr., M.D., Assistant Clinical Professor
of Medicine

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MEDICINE

Pulmonary Diseases and Pulmonary Physiology

Wednesdays 12:00 P.M.-1:15 P.M.

Radiation Center Conference Room, Hospital of
St. Raphael, New Haven

Chairman: John B. Berte, M.D., Director, Depart-
ment of Pulmonary Diseases and Inhalation
Therapy, Hospital of St. Raphael

Open to all physicians

Hematology

Thursdays 1:30 P.M.-3:30 P.M.

Hematology Laboratory and Wards, Hospital of
St. Raphael, New Haven

Robert P. Zanes, Jr., M.D., Attending Physician
In Medicine, Hospital of St. Raphael

Open to all physicians

GENERAL MEDICINE

March 5 9:30 A.M.-4:00 P.M.

Symposium on Automobile Accidents and Trauma
Mary S. Harkness Memorial Auditorium, Yale
School of Medicine

Sponsored by the Departments of Pathology and
Surgery, Yale School of Medicine

Speakers: Allen Moritz, M.D., Provost of Medical
Affairs, Case-Western Reserve University; John
H. Davis, M.D., Department of Surgery, Case-
Western Reserve University; Paul Gikas, M.D.,
Department of Pathology, University of Michi-
gan Medical School; Colonel John P. Stapp, U.S.
Air Force Medical Corps, National Highway
Safety Bureau.

Contact: Michael Kashgarian, M.D., Department
of Pathology; Kristaps J. Keggi, M.D., Depart-
ment of Surgery, Yale School of Medicine

No registration fee, open to all physicians

March 28-29

3rd National Congress on the Socio-Economics of
Health Care

Palmer House, Chicago

Sponsored by the American Medical Association
No registration fee

April 24-26

30th Annual Session of the American Academy of
Physical Medicine and Rehabilitation

Palmer House, Chicago

Program designed "to enhance the training of residents in PM&R who are preparing for examinations to qualify as specialists and to refresh and update the knowledge of those who have been pursuing the specialty."

Registration fee, \$20 members, \$25 nonmembers; send to American Academy of Physical Medicine and Rehabilitation, 30 North Michigan Avenue, Chicago, Ill., 60602

PSYCHIATRY

Seminars sponsored by the Connecticut Valley Hospital, Middletown; meetings held in Merritt Hall Auditorium

Visiting Faculty: Connecticut Postgraduate Seminar

February 11 10:30 A.M.
The Therapeutic Management of the Sociopath,
John Donnelly, M.D.

February 20 10:30 A.M.
Alcohol and Drug Dependency, Ruth Fox, M.D.
Chairmen: Iago Galdston, M.D., Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology, c/o Fairfield Hills Hospital, Newtown; Sal A. Prins, M.D., Director of Training, Connecticut Valley Hospital.

Doctor's Office

Anthony J. Arena, M.D., announces the opening of an office for the practice of general surgery at 195 South Main Street, Middletown.

Ronald J. Czaja, M.D. and William A. Schear, M.D., announce the opening of an office for the practice of obstetrics and gynecology, in partnership with Robert J. Gfeller, M.D. at 14 East Main Street, Stafford Springs.

Alan H. Goodman, M.D., announces the relocation of his office for the practice of orthopedic surgery to 2 Church Street South, Suite 401, New Haven.

W. Ames LaPan, M.D., announces the opening of an office for the general practice of medicine in the Tolland Professional Building, Route 74, Tolland.

John A. Muccino, M.D., announces the opening of an office for the practice of obstetrics, gynecology and infertility at 140 Woodland Street, Hartford.

Charles G. O'Connell, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 57 Union Street, Vernon.

Placement Opportunities

PEDIATRICIAN for a rapidly growing community in Western Connecticut. Present pediatrician wants to concentrate solely on subspecialty. Arrangements on solo, salary or associate basis.

EMPLOYEES' PHYSICIAN—physician for employees' clinic, whose duties would consist of pre-employment and annual physical examinations, daily sick call, and occasionally immunizations, hours from 8:00 A.M. to 5:00 P.M. with an hour for lunch, Monday through Friday. Four weeks' vacation after one year and excellent fringe benefits. Salary of \$20,000 per annum.

PEDIATRICIAN—Three member partnership in Obstetrics and Gynecology is looking for a pediatrician for the Enfield, Connecticut area which serves a population of 60,000. An office is immediately available in a new air-conditioned medical building.

WANTED: PSYCHIATRIST—Opportunities exist in State Welfare Department for (1) a Psychiatrist to administer and coordinate the Mental Health Program; (2) Psychiatrists to act as District Welfare Department Consultants for the Mental Health Care Program. Contact: Orvan W. Hess, M.D., Medical Director, State Welfare Department, 1000 Asylum Avenue, Hartford, Connecticut 06115.

ONE YEAR PSYCHIATRIC RESIDENCY at 3rd year level for year beginning July, 1969. AMA approved. Unique opportunity to prepare for private practice and community psychiatry. Supervised intensive, dynamically oriented psychotherapy emphasized. Experience in meaningful application of psychopharmacological agents and somatotherapy. Work with adults and children in residential and out-patient setting. Stipend \$15,000 per annum, with major medical insurance benefits. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

G.P.—Office space available with established physician, general medicine, spending half-time writing. Association and eventual partnership. Excellent schools and municipal facilities. Fairfield County.

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BOOK REVIEWS

MEDICAL PHYSIOLOGY, 12th Edition. Volumes I and II. Edited by Vernon B. Mountcastle, M.D. The C. V. Mosby Company, St. Louis, 1968. Illustrated. \$24.00.

Reviewed by: LOUIS H. NAHUM

This is the most comprehensive, most current evaluation of the application of physiological methods in the study of disease. It is written by 31 eminent contributors but its overall excellence reflects Professor Mountcastle's careful editing. For ease of reference each volume contains the complete detailed 38 page index. One will find in these volumes the latest data on hemodynamics, fluid balance, thirst.

No body of knowledge is advancing more rapidly than human physiology and nothing is more vital to today's and tomorrow's physician than a clear understanding of modern physiology. Physiology today must bridge the distance from cellular biology on the one hand to systems analysis and control theory on the other. Perfect examples of this approach can be found in the treatment of internal homeostasis reaction to our environment and action upon our environment.

This new edition has been completely revised. It has been expanded from one to two volumes, from 72 to 80 chapters. Twenty-nine of these chapters are wholly new and 45 have been extensively revised by either the original or new authors. Of the 880 illustrations more than 350 are new to this edition. These two volumes are superb. The student, the clinician and the research scientist will find in them an immense store of meaningful, practical, timely information. The facts, principles, concepts and approaches to medicine are fundamental and vital to every area of modern medicine. It is applicable to all medical problems, and can be extraordinarily valuable to those who must evaluate theories and concepts in physiological bases of medicine.

The two volumes because of their precise statements and logical development of concepts may very well become a source for programming and computer teaching of special areas in physiology.

The book is beautifully printed, two columns to a page and without a recognizable flaw.

SPARE-PART SURGERY: THE SURGICAL PRACTICE OF THE FUTURE. By Donald Longmore, Doubleday & Company, Inc., New York. 192 pages. \$5.95

Reviewed by: IRA S. GOLDENBERG

The physician's dream of replacing worn-out parts of the human body has become reality during the past decade and it is obvious that further dramatic progress in the field of transplantation is imminent. The average physician and the educated lay person are most often on the fringe of understanding the intricacies of techniques involved in major organ transplants and Dr. Longmore, a Fellow of the Royal College of Surgeons in Edinburgh, who has been engaged in surgical research at the National Heart Hospital, London, has written a book aimed at these two groups. It is not a book for the average lay person since it presupposes some

scientific background, but the explanations are lucid enough that even a non-physician can learn a great deal about extracorporeal machines, prosthetic limbs, mechanical implants and homograft techniques.

This slim volume opens with a clear explanation of present knowledge of the important immune mechanisms and rejection phenomena involved in "spare-part surgery". Superb color and black and white drawings and photographs are profuse and aid the reader at every turn of a page. The author's philosophy permeates each section and his intense interest in his subject is obvious. He discusses not only accomplishments, but also devotes many pages to what need to be done in the future, and to current research in his own and other laboratories. The book crosses political boundaries freely, as a true scientific work should, and the efforts and deeds of scientists throughout the world are detailed.

This is the eighth of The Doubleday Science Series. Previous volumes have covered such topics as lasers, plastics, metals, ceramics, glass, road engineering and management science. The books are printed beautifully by a photo offset process which keeps the cost at a reasonable level. For even wider circulation, paper back editions are available. Doubleday has rendered an extremely valuable service in publishing this science series and *Spare-Part Surgery* is highly recommended to all readers.

PHYSICAL STANDARDS IN WORLD WAR II—Prepared and published under the direction of Lt. General Leonard D. Heaton, The Surgeon General, U.S. Army. Editor-in-Chief, Colonel Robert S. Anderson, M.C., U.S.A. Office of the Surgeon General, Department of the Army, Washington, D.C. 1967. 356 pp.

By: GERALD I. PITEGOFF

This book presents the United States Army's standardized procedure for medically classifying men who were candidates for induction in World War II.

In this well bound, nicely printed volume, the responsibility to recruit and maintain an effective defense organization is defined. A brief historical account of the development of physical standards for acceptance of men and later women in the Armed Forces, including an appendix of mobilization regulations, is presented.

The goal, and this the guiding philosophy of the War Department, is the making available every supply of manpower with minimal financial or medical burden to the country and jeopardy to the health of individual and others.

Qualifications for services were dynamically re-evaluated during the period between World War I and World War II. The selective service training act of 1940 constituted the basis of physical standards for the induction of men and women into the Armed Services during World War II. These standards are included in this volume.

A comparison of the physical standards in World War II and the present standards is indicative of the changes in medical practice. A single example, the use of the audiometer versus the whisper test, reflects these changes.

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COMPREHENSIVE TEXTBOOK OF PSYCHIATRY.
Edited by Alfred M. Freedman, M.D., Harold I. Kaplan, M.D. and Helen S. Kaplan, M.D., Ph.D., Assistant to the Editors. The Williams & Wilkins Company, Baltimore, 1967. 1666 pp. \$24.75.

Reviewed by: STEPHEN FLECK

Comprehensive indeed describes this oversize volume of 1666 pages arranged in two columns. The sheer magnitude of this work arouses awe, and the editors have succeeded, not only with regard to comprehensiveness, but also in organizing such a vast array of material into eleven "areas" with varying numbers of chapters in each area. These areas are: history of psychiatry; basic behavioral sciences; current theories of personality and psychopathology; neurology; assessment in psychiatry; psychiatric syndromes; psychiatric treatment; child psychiatry; community and social psychiatry, psychiatric sub-specialties, and fields related to psychiatry.

The glittering array of 174 authors includes two dozen chairmen of academic departments of psychiatry besides many other outstanding representatives of psychiatry and of the related behavioral sciences. Even though there are some chapters which could have been improved upon, uniformity, especially uniformity of excellence throughout such a volume cannot be expected. Nor can it be expected that one reviewer can be sufficiently comprehensive in his knowledge or understanding of some of the sub-specialties to judge all this material competently. To this reviewer the chapters on Electrical Activity of the Brain (Doty and Smith), The Limbic System (Doty), on Motivation (Malmö), Ethology (Hess), and on Development of Community Psychiatry Concepts (Caplan and Caplan) stand out, and the ones on Psychosomatic Medicine are excellent.

Comprehensiveness also characterizes the editors' intent to present all important viewpoints where differences in approach or conceptualization exist. In addition, an ingenious system of cross referencing within the volume helps the reader to check relevant aspects of a topic or chapter within the volume itself.

Therefore this is an eclectic resource volume which belongs on every psychiatrist's shelf and it should also prove useful to medical students and non-psychiatric physicians, and especially so to the young psychiatrist preparing himself for specialty examinations.

ANESTHESIA FOR INFANTS AND CHILDREN. Third Edition. By Robert M. Smith, M.D., Anesthesiologist, Children's Medical Center, Boston, Mass., Pp. 530, with 240 illustrations. Cloth. \$17.50. The C. V. Mosby Company, Saint Louis, 1968.

Reviewed by: JOHN D. MURPHY

As Dr. C. R. Stephen hopefully prophesized in his 1964 review of the Second Edition, Dr. Smith has completed his new edition almost on an "every four year" schedule. In any case, it remains one of the few outstanding texts in the specialty.

The present volume puts the accent, as in previous editions, on safe and sane anesthetic administration to the young. And herein lies its reward to the reader. Attention to detail, fully exemplified in the writing, is the key to the principles of practice. A nice balance of reiteration and updating bring the latest thinking into sharp focus. The trite is

the tried and true, flowing naturally from the wealth of material at the author's disposal.

Many of the thirty one chapters have been expanded, in particular, those devoted to respiratory physiology, ventilatory problems and open-cardiac surgical procedures. A new section on metabolic response to surgery emphasizes the prevention of acidosis by the use of non-rebreathing techniques in the small infant. The role of catecholamines and brown adipose tissue in temperature regulation in the neonate has been added. The chapter on respiratory physiology has essentially been rewritten, and the addition of material on respiratory symbols, ventilation-perfusion relationships and neonatal respiratory adaptation has helped to solidify this vital topic. The trend away from ether toward the halogenated agents is emphasized. The place of the neuroleptic drugs in the management of children is felt by the author to be still uncertain.

There are several references to hyperbaric techniques, both intra-operative and post-operative. Sections relating to anesthesia for the premature and newborn infants are presented in their previously excellent fashion. The newer method for handling infants with omphalocele (staged repair) is discussed. Congenital cardiac lesions and their anesthetic management are handled thoroughly, and the accompanying endotracheal intubation vs. tracheostomy are discussed. Emergency resuscitation as well as long-term respiratory support are well-treated in chapters 28 and 29, both of which are updated over the previous edition. The section on induction of general anesthesia is one of the best in the book and abounds with the "pearls" and reminders so helpful in our day-to-day handling of youngsters. The chapter on mortality, as always, makes interesting reading while the lesson and the challenge are obviously clear.

The bibliography, tables and figures are considerably enlarged. The volume is well-bound and easily readable. This then is a clear-cut "must" for all the varied talents administering anesthetics to children. Dr. Smith's contribution to the specialty should always be close at hand.

FAMILIAR MEDICAL QUOTATIONS. Edited by Maurice B. Strauss, M.D. Little, Brown and Company, Boston, 1968. 968 pp. \$15.00

Reviewed by: HARRY G. MOSS, M.D.

With respect to title, and arrangement of material, *Familiar Medical Quotations* by Dr. Maurice B. Strauss is remarkably reminiscent of *Familiar Quotations* by John Bartlett. Bartlett's, first issued in 1855, has now gone through 14 editions. There is every reason to predict that Strauss's book will adorn the library of just about every student and practitioner of medicine and affiliated callings, for generations to come.

It is noteworthy that the publisher of Dr. Strauss's book is Little, Brown and Company, of which John Bartlett was a partner. Bartlett, in his selection of quotations, included those which he thought "familiar or worthy of being familiar". Strauss has done for medicine and its lore what Bartlett did for universal literature.

Strauss's volume, like Bartlett's, has two separate indices, one by author and the other by key words, which are used to locate phrases and ideas.

In addition, there is an alphabetical table of contents, with over 400 subject categories. To name only a very few in alphabetical order: Anatomy, Bedside Manner, Consulta-

tion, Discovery, Experimental Medicine, Frostbite, etc. etc. Each section contains quotations in chronological order, so that the reader may always have a historical perspective. For example, the section on Old Age has quotations from (in this order), Sir Thomas More, Shakespeare, Metchnikoff, Osler and Maugham, and so on to the ubiquitous Anonymous. This short list of names will convey the eclectic composition of the book.

As the preface indicates, the quotations are from writings by doctors, about doctors, in favor of doctors, against doctors, etc.

A few brief examples from this smorgasbord of medical wit and wisdom will help to suggest the flavor:

Concerning Diagnosis and Terminology: "Physicians think they do a lot for a patient when they give his disease a name." (Immanuel Kant) . . . "None of us is infallible, not even the youngest of us." (J. Chalmers DaCosta) . . . "If you have to choose between a brilliant and a common sense diagnosis, your percentage of correct ones will be much higher with the latter." (Charles Norris) . . . "Idiopathic epilepsy is idiopathic ignorance on the part of the doctor." (Martin H. Fisher)

Bits on *Treatment:* "Old age is a disease which we cannot cure." (Seneca) . . . "Take a dose of medicine once, and in all probability you will be obliged to take an additional hundred afterwards." (Napoleon Bonaparte) . . . "It is better to shoot the patient than to shoot the works." (Hugh Cabot) . . . "It is difficult to make the asymptomatic patient feel better." (Stanley O. Hoerr)

Some advice on *Prognosis:* "If the news must be had, tell it soberly and promptly." (Sir Henry H. Bashford)

Wry remarks on *Anatomy:* "Gentlemen, damn the sphenoid bone!" (Dr. Oliver Wendell Holmes) . . . "Diaphragm, n. A muscular partition separating disorders of the chest from disorders of the bowels." (Ambrose Bierce, *The Devil's Dictionary*)

Concerning *Textbooks:* "It is a most gratifying sign of the rapid progress of our time that our best textbooks become antiquated so quickly." (These words were written by Theodor Billroth, 1829-1894).

Two remarks by doctors about *Doctors:* "The face of a physician, like that of a diplomatist, should be impenetrable." (Dr. Oliver Wendell Holmes) . . . "As with eggs, there is no such thing as a poor doctor, doctors are either good or bad." (Fuller Albright)

An acerbic quote on *Science* by George Bernard Shaw: "Science is always wrong. It never solves a problem without creating ten more." (What a glorious time he would have had if he had lived to see the host of troubles engendered by pesticides, antibiotics and thalidomide.)

An old Spanish proverb comments on *Woman:* "Six men give a doctor less to do than one woman."

And finally, a newspaper heading, in the section on *Epitaphs:* "John Longbottom, Aged 3 Months, Dies . . . Comment from *Punch:* *Ars longa, vita brevis.*"

There has been room here to exhibit only a few of the nuggets to be found in *Familiar Medical Quotations*. This book is a veritable Fort Knox of medical wisdom and mirth. It is a rare combination of instruction and entertainment, and should prove an ideal gift for any colleague, student, or any layman who is even slightly interested in medicine.

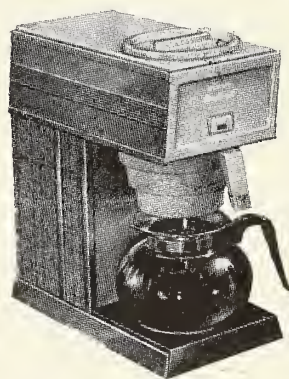
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Handbook of Pediatric Medical Emergencies. 4th Edition. Edited by Charles Varga, M.D. and Contributors. The C. V. Mosby Company, St. Louis, 1968. 694 pp. with 120 illustrations \$19.75.

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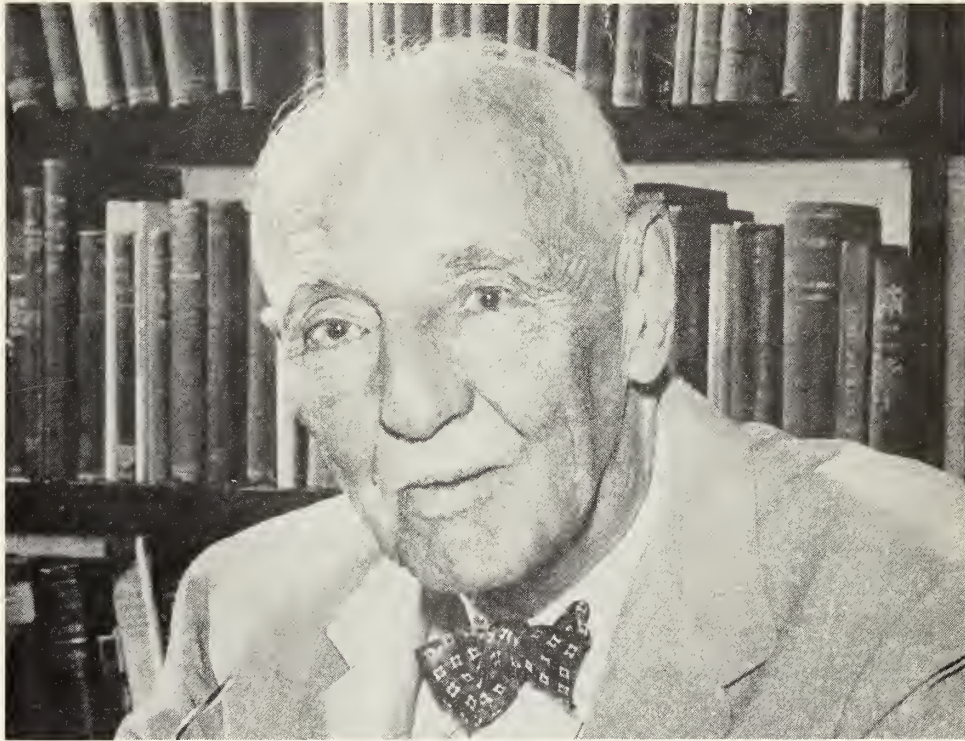


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Connecticut Medicine

editorials

Obtaining Personal Health Care

"I dream things that never were and I say why not?"—G. B. Shaw.

Seventy years ago personal health care was a privilege, today it is considered a right. Only a few physicians then were specialists, today an overwhelming number are college graduates, who have engaged in prolonged post-graduate training and practice in specialized fields. This had led to a scarcity of good personal health care, in rural health care and now in the core cities. Despite the magnificent facilities available for specialized procedures that were unimaginable in 1900, the problem of how to obtain health care whether corrective or preventive urgently requires solution.

Several commissions of learned men, medical specialists educators and representatives of the public have studied the problem.¹ All recognize that the prototype of general practitioners of the 19th century who could do "everything" by virtue of the fact that almost nothing could be done well, could not be revived. They saw clearly that there was an urgent need for health personnel to whom the public could readily turn for its most common and pressing even if undramatic medical needs. They named such personnel generalists, primary physicians and family doctors and outlined the nature of their necessary basic training in general medicine, emergency care, geriatrics, pediatrics and psychiatry.

The question is, however, how do we make the careers of such physicians attractive enough to induce medical students to chose this path. Perhaps we could have learned something if the commissions had included medical students and a few general

practitioners whose doctor sons are probably all going into medical specialities. At any rate the trend toward specialization by medical graduates has not been reversed. Rather the opposite—fewer indicate a desire to enter even general internal medicine and surgery and more seem to indicate a preference for specialized areas within these specialties. After four years of medical school, three to four years of hospital training and at least two in the military, it is not difficult to understand why the career of the primary physician offers too little intellectual, financial and status rewards to be attractive. We can't "indenture" medical students and we can't conscript them for such careers. What alternatives are there.

One approach is the health personnel team now being tried out in various disadvantaged regions. One of their functions would be "preventive" which begins when a newborn infant leaves the hospital and includes baby care, hygiene, nutritional advice, immunizations, and a host of other minor services for persons who do not perceive any deviations from what they consider "normal." Although invaluable, such services do not necessarily require a physician. But since the personnel rendering these services are in constant communication with physician members, the recipients of these services will feel comfortable. Prototypes of these services are found in school and industrial nurses.

When a person recognizes "something wrong" with him, he should consult the physician member of the team, who must then after an examination decide whether the symptoms are minor or major enough to be incapacitating and also whether there is no treatment that will affect the outcome and whether there is. Examples of the former are acute

ABOUT THE COVER

Professor Charles-Edward A. Winslow

Professor Charles-Edward A. Winslow was for more than thirty years one of the nation's and the world's foremost promoters of public health. From the founding of the Department of Public Health at Yale in 1915 to his retirement in 1945 he was deeply concerned with the application of the health sciences to society. His impact on this field as an educator has been felt by several generations of public health workers and his ideas are very much in evidence in today's concern with the organization and delivery of health services.

upper respiratory infections not complicated by purulent sinusitis or otitis media or untoward reaction to drugs. In this same category are diseases ultimately fatal regardless of palliative procedures such as metastatic carcinoma. Prompt diagnosis and treatment may enhance the patient's ability to function and perhaps his longevity but not the eventual outcome.

In the second category of disorders are those for which there are specific or at least definite means of treatment that do alter the outcome. In some, prompt recognition and treatment can influence duration of illness and suffering. Anemias, calculi, several endocrine disorders, recognition of early tuberculosis are examples. There are also disorders in which prompt recognition and treatment is of the utmost importance to life itself. Pneumococcal pneumonia, meningitis, acute appendicitis, intestinal infarction, subacute bacterial endocarditis, acute glaucoma, Addisonian crises, perforated ulcer, myxedema coma, myocardial infarction with arrhythmias, easily come to mind and many others as well.

The primary physician then is to recognize the disorders in which time is truly of the essence and to ensure that such patients receive promptly the specialized treatment required and where they must be obtained. A physician working long hours in solo practice in the care of many illnesses that are not crucial with his intellectual and technical tools numbed by lack of stimulation cannot encourage young physicians to enter this kind of practice. This is why young physicians are shifting away from solo practice to specialization, away from a life in which 90 per cent of their work is irrelevant to a more meaningful type of medical activity.

An alternative approach is that of the Health Team, to include nurses-aides, social workers, secretaries, technicians and physicians who are in daily and direct partnership with the specialists most frequently needed for the patient group to be serviced who would share responsibility for these patients both inside and outside the hospital. By working closely with specialists in the care of the more critically ill patients the primary physician will retain and increase the clinical skills needed to meet the vital task of recognizing critical situations, to develop some subspecialty skills and to enhance his overall competence.

In such a team many of the functions of the primary physicians could be done by others under his tutelage and supervision. A preliminary history could be done readily by a non-physician allowing the physician to concentrate on and amplify the im-

portant relevant aspects. The physician could devote his time to the questions and deviations from normal. A nurse could handle many of the minor ailments much as a mother does. In the smaller urban and suburban areas the community hospital would serve as the base for primary health teams as well as for the highly specialized services thus combining and associating the primary and specialized functions to the advantage of both physician and patient. In the larger urban areas the unit might revolve around the medical center with satellite clinics serving as primary care loci in disadvantaged areas of the core city and staffed by physicians who would directly care for their patients in the hospital when needed.

When we can work a scheme that permits a close working relationship on an equal basis between the primary physician and specialist, then this might offer the intellectual and financial status and satisfactions needed for recruitments of the primary physician, so that primary personal health care will not be isolated from the necessary stimulus and challenge that hospital practice so well provides.

In the meanwhile the New Haven County Medical Association is planning to establish an evening clinic in the Fair Haven district of New Haven to be staffed by volunteer physicians with the aid of local Public Health Nurses and other paramedical personnel to render good primary medical attention with referral of special care problems to appropriate practicing physicians. This pilot experiment of making good health care available to the community is an outgrowth of the widespread need for primary care physicians and an experiment by organized medicine in how best to obtain personal health care. It is clear we must bridge the gap between the present scarcity of physicians rendering personal health care and the time in the future when the primary physician will be more readily recruited from medical students by such "dreams" as were considered above.

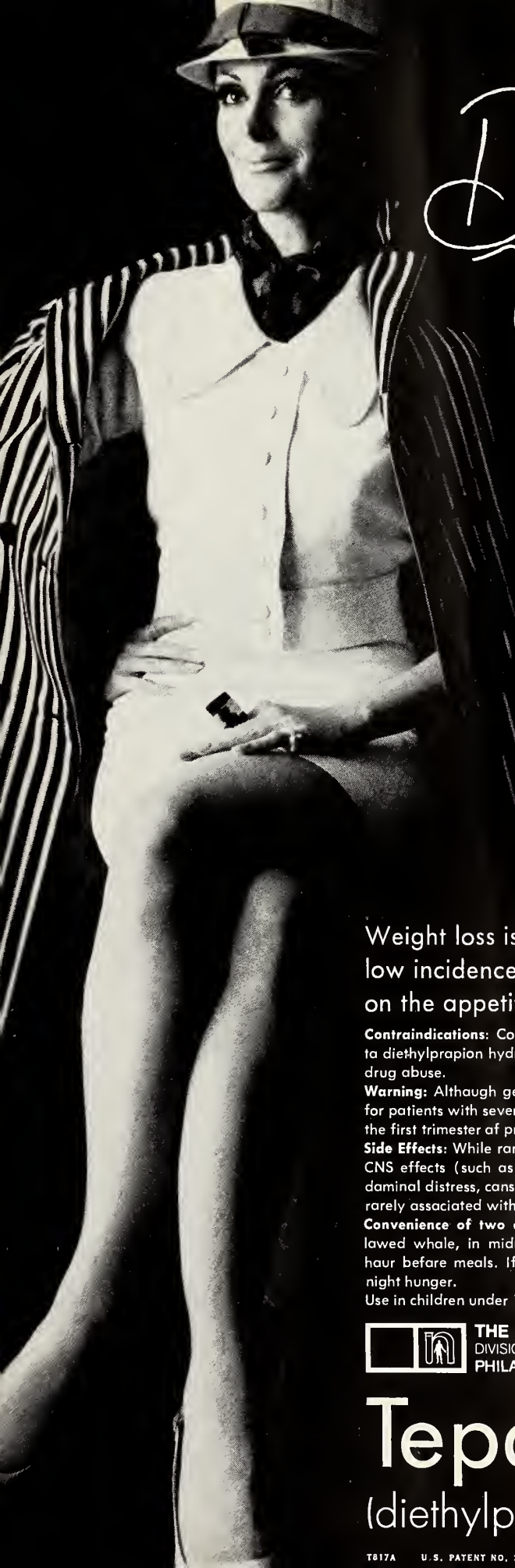
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Reference

1. Strauss, M. B.: The unsolved problem: obtaining personal health care. *New Eng. J. Med.*, 279: 831, October 10, 1968.

Physiologic Adjustments To Anemia

A red cell mass less than normal reduces oxygen carrying capacity of the blood. Mechanisms that attempt to compensate for this decrease are tachycardia, hyperpnoea, increased cardiac output and



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accelerated rates of blood flow secondary to decreased blood viscosity, and peripheral resistance. Such responses, however, depend on the rate at which the red cell mass decreases, the magnitude of the anemia and the oxygen requirements of the anemic subject—that is the levels of physical and metabolic activity. If the anemia develops gradually, an otherwise normal person can tolerate as much as 50 per cent reduction in red cell mass without conspicuous untoward effects.

However, acute hemorrhage with rapid loss of as little as 30 per cent of the body's hemoglobin may evoke a profound reaction with circulatory collapse. Thus the immediate effect of acute hemorrhage is a decrease in total blood volume due to equivalent decrements in both plasma and cells. At first the peripheral erythroid values do not reflect the blood loss. Then extravascular fluid begins to enter the intravascular compartment and this corrects the hypovolemic state. The venous hematocrit value, hemoglobin level and erythrocyte count may be normal immediately after an acute hemorrhage despite a substantial reduction in red cell mass.

In response to hypovolemia, cardiac, pulmonary, and vascular adjustments are brought into play to prevent circulatory collapse and to maintain blood supply to brain and heart. Clinically such physiologic corrective mechanisms produce tachycardia, hyperpnoea, and cold skin. If these adjustments are unable to cope with the hypovolemia, then cardiac output decreases, blood pressure falls and shock ensues. Treatment of this phase of an acute hemorrhage should be aimed at correcting the hypovolemic state and if necessary by transfusions.

After the acute bleeding stops blood volume is usually restored to normal within twelve to thirty-six hours. The speed with which extravascular fluid enters the vascular compartment depends upon the subject's state of hydration, but also on the rate at which new protein is added to the circulation. If the nutritional status is satisfactory replenishment of plasma proteins begins at once and occurs much faster than regeneration of hemoglobin. As plasma volume increases the reduced cell mass is diluted and even though all bleeding has ceased the peripheral, erythroid values (hemoglobin, hematocrit value and red cell count) decrease and continue to decrease until the blood volume becomes normal. At this stage of normal blood volume, transfusion of red packed cells constitutes the replacement therapy of choice if any blood transfusion is deemed necessary. If whole blood transfusion is employed at this stage it will produce hypervolemia and may pre-

cipitate serious consequences especially in patients with underlying cardiac disease who cannot tolerate expanded blood volume.

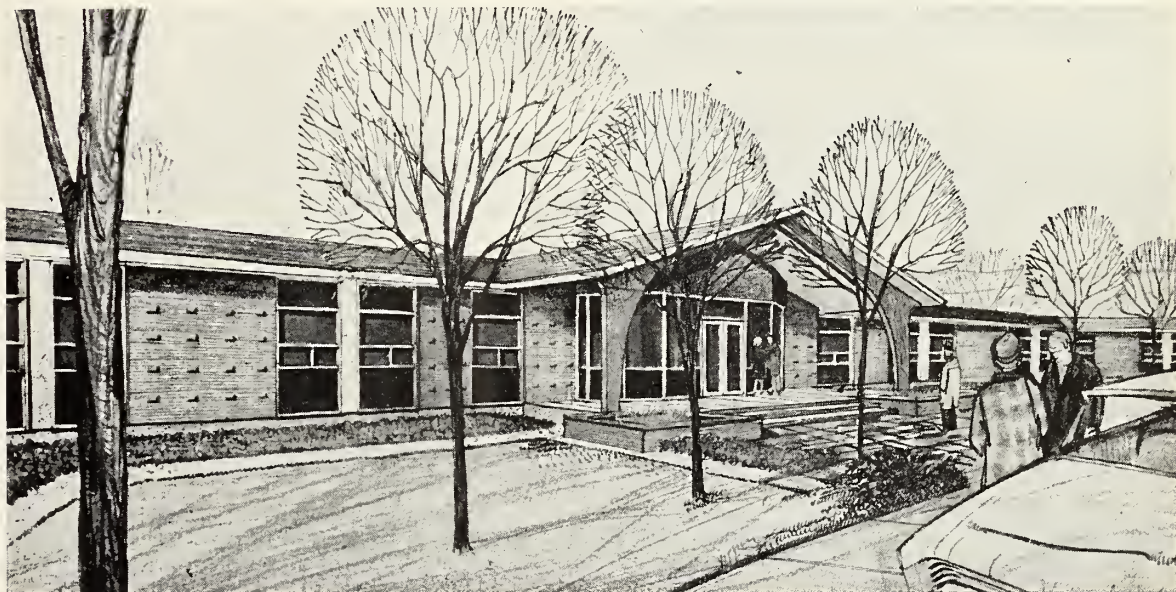
Ordinarily if anemia develops gradually the body is able to compensate for it amazingly well. Long standing anemia with hemoglobin values of 9-10 grams per 100 ml. causes little or no dysfunction manifesting only minimal pallor and slight tachycardia. Exertional dyspnoea begins when hemoglobin concentration is about 7 grams and dyspnoea at rest at about 3 grams and heart failure at 2-2.5 grams per 100 ml. Appreciable weakness usually does not appear until the hemoglobin falls to 6 grams per 100 ml. or less. Those who cannot correct for this deficiency do not tolerate so well a decrease in the oxygen carrying capacity of the blood. Children and young adults often deny all symptoms even in the face of marked anemia. Patients with underlying heart disease on the other hand may develop myocardial ischemia or even myocardial infarction with minimal or moderate anemia.

The responses to anemia are also influenced by oxygen requirements. For example a red cell mass that is quite adequate for an elderly sedentary person may be quite inadequate for a young physically active male. In addition metabolic activity affects the physiologic and pathophysiologic responses to a decrease in circulating hemoglobin. For example a person with hypothyroidism and a concentration of hemoglobin of 10 grams per 100 ml. does not manifest increased heart rate and cardiac output because his reduced red cell mass is adequate to supply enough oxygen to meet decreased cellular needs. On the other hand this degree of reduced hemoglobin in a patient with fever, or hyperthyroidism might cause significant symptoms due to the anemia.

The clinical consequences of an anemia are the same irrespective of its origin. However the effects of anemia are often obscured or complicated by other manifestation of the primary disease such as neuropathy of vitamin B₁₂ deficiency, thrombotic complications of sickle cell anemia, the neutropenia and thrombocytopenia of hypoplastic anemia and the frequent changes of hemolysis. For these reasons the clinical pictures of the various anemias differ strikingly despite similarities in the physiologic responses and pathophysiologic effects of a decrease in red cell mass.

In a normal person reduction in red cell mass is a potent stimulus to the bone marrow. Increased numbers of undifferentiated cells enter the erythrocyte compartments. If there is an adequate nutri-

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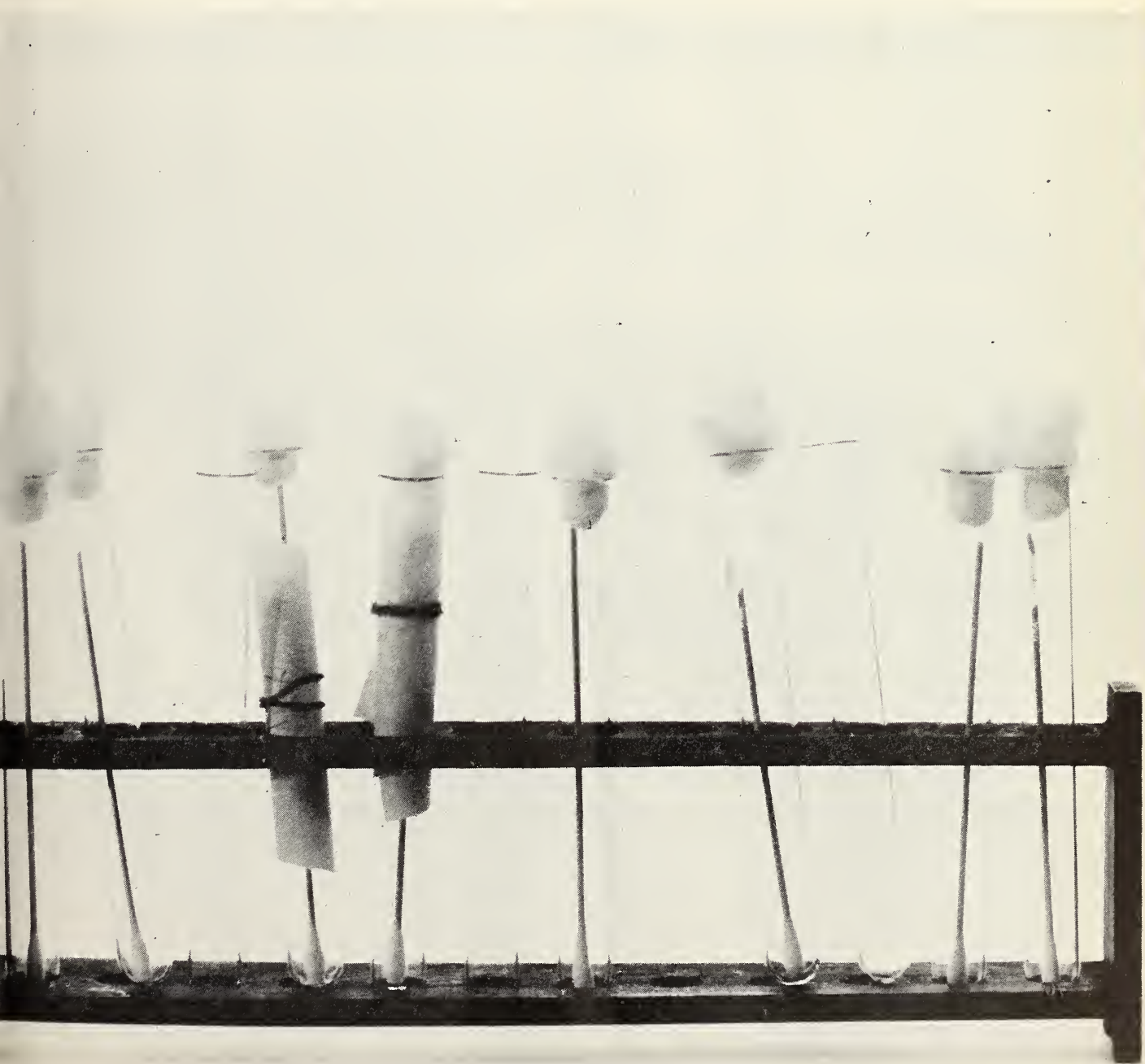
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tional and hormonal environment, then proliferation and maturation of erythrocyte precursors proceed in an orderly fashion. In response to a sudden potent stimulus some cellular divisions may be missed and some young erythrocytes will be released prematurely into the circulation. In general, however, the normal ratio of immature to mature nucleated erythrocytes is maintained and the erythrocyte generation time is not altered.

The quantity of red bone marrow increases and aspirates of marrow reveal erythrocyte regeneration. Polychromasia, reticulocyte counts of 5-15 per cent and circulating nucleated red cells of 1-5 per cent 100 leucocytes appear in the peripheral blood within one to two days. Of course the magnitude of these findings is determined by the severity of the hemorrhage. Ordinarily the reticulocyte count reaches a peak in seven to ten days and then gradually subsides. If all requirements of erythropoiesis are met and hemorrhage does not recur, the red cell mass is restored to normal within four to eight weeks.

L.H.N.

Reference

1. Linman, J. W.: Physiologic and pathophysiologic effects of anemia. *New Eng. J. Med.*, 279: 812, October 10, 1968.

Nutrition Of The Fetus And The Intelligence Of The Child

Striking data obtained from a collaborative Perinatal Research Project of the National Institute Neurological Disease and Blindness (NINDB) provides evidence that malnutrition in the mother during the gestational period can impede the eventual intellectual achievement of the child. That malnutrition in the mothers does have serious effects on her offspring can be gleaned from the fact that 95 per cent of the babies born in a Columbian village became mentally retarded by the time they are teenagers because of inadequate diet.

In the collaborative study the results of which were presented to NINDB more than 60,000 women and 55,000 children born to them between 1959 and the end of 1965 participated. Fourteen major medical centers have cooperated in the research which will continue until the children concerned are well along in school. All the project children have been newborn eight months and one year. Neurological examinations and more complete findings are available in several thousand youngsters

born during the first year of the study who are now seven or eight years of age. Many though not all of the children were born into disadvantaged homes.

What the findings suggest is that malnutrition in the mother, whether due to inadequate diet or metabolic derangements resulting from hypertension or diabetes has a quantifiable impact on the central nervous system of the child. A striking example comes from a study of identical twins. In the 50's Dr. John A. Churchill already made the observation that the twin who is smaller at birth generally reaches an I.Q. level an average of eight points lower on the Stanford-Binet scale than its brother or sister presumably because it has had less nourishment in-utero. Measurements of some 500 sets of monozygotic twins in the NINDB study have now confirmed this finding that twins are generally less bright than their singly born siblings.

The NINDB study also looked into the intelligence of children born to mothers with hypertensive cardiovascular disease and diabetes mellitus. Patients with these disorders were compared to controls carefully matched as to age, ethnic origin and socioeconomic factors. In a group of 127 children born to women with hypertension, many of whom developed toxemia of pregnancy, the average I.Q. was 7.2 points below that of children born to normotensive controls. Of 121 children born to diabetic mothers who at one time or another during pregnancy showed acetouria, the average Binet I.Q. was some 6 points lower than those born to diabetics who did not manifest this sign during the gestational period. Protein deprivation traceable to metabolic imbalance was cited as the probable cause.

The findings in diabetics are particularly significant because acetouria was found both in these expectant mothers as well as in those whose amino-acid blood levels were less because of protein-calorie deprivation. In experimental rats one can produce a scarcity of nutrients in the mother's diet which causes her body to turn to its own fat and proteins as fuel because sufficient carbohydrates are not available. In humans if the mother is a diabetic it is her disease which is primarily to blame. But much the same can happen to a pregnant woman who lacks enough of the proper foods to eat.

The presence of acetouria is the sign that only second-class raw materials are available to the fetus and these lead to impairment of central nervous system development. Among poor black women who were not diabetic as among other women in the NINDB study group, the shabby nutritional state of many women from the ghetto may be one reason

why their children do poorly at school. Genetic status being equal the evidence indicates that malnutrition in-utero is as close as science has come to explaining class differences on sound biological terms. What lends weight to this view is that the testing began at the age of eight months before cultural influences begin to exert their effects.

There are two ideas that this work brings into question. One is that the fetus will take whatever nourishment it needs regardless of what the mother eats. The second is that hypoxia-anoxia from collapse of the umbilical cord or some other birth trauma is what causes a preponderance of neurological defects rather than maternal malnutrition. Perhaps we have been too preoccupied with obstetrical events at labor and delivery and too little with malnutrition in-utero. Infants weighing less than 2,500 grams at birth whether premature or full-term are indeed likely to have subnormal I.Q. independent of their socioeconomic or ethnic origin. It is whether the infants have suffered nutritional deprivation in-utero for whatever the reason that seems to determine their intellectual capacity after birth.

Malnutrition may also be the central factor in the development of spastic diplegia the most common cause of cerebral palsy. Of 162 babies in the study who weighed less than four pounds at birth forty-eight have shown definite signs of this disorder. The working hypothesis to explain this finding is that malnutrition during gestation so dehydrated the fetus that circulatory difficulty and hemorrhage in the mid-veins of the brain ensued which prevented the development of proper motor function later on.

What can be done to diminish the rate of central nervous system impairment of the newborn? Clearly better prenatal care is called for particularly among the poor. What is new about the collaborative study is that better knowledge of nutrition may make possible prescriptions on dietary advice more sophisticated than are employed at present. Also that daily urine testing to detect even transient acetonuria due to infection, fever, or other causes can lead to prompt remedial measures to protect the fetal brain.

The time has clearly arrived when man can control at least one factor in the intelligence of the fetus and make significant improvement in the I.Q. of a child by improved prenatal care which will avoid malnutrition of the fetus.

L.H.N.

Reference

1. Randal, J.: Biological nutrition. *Bio Science*, 18: 507, June 1968.

Science Tools: 32. The Phaco-Emulsifier In Cataract Surgery

The phaco-emulsifier is a titanium alloy hollow needle which vibrates at an ultrasonic frequency of 40,000 times a second. Around the one millimeter diameter needle is a protective jacket of silicone. Between the outer wall of the needle and the protective sheath there is a constant flow of irrigating fluid. The outward flow of fluid and the emulsified lens material is through the center of the ultrasonic needle, while suction is controlled by a second foot switch.

The emulsification of the cataract must be performed with the use of an operating microscope and the patient's eye must first be dilated to seven millimeters. Then a two millimeter shelved incision is made in the limbus. After the aqueous humor has escaped or been aspirated, air is injected into the anterior chamber to completely expose the anterior surface of the lens to air. Under the microscope a cytome knife is then passed across the anterior capsule and cuts away a V shaped portion.

The nucleus and parts of the cortex are gently maneuvered out of the capsule and irrigating fluid instilled. Short bursts of energy are now used to emulsify the nucleus and cortical material while aspirating it from the eye at the same time. The remainder of the anterior capsule can be easily withdrawn following irrigation with an enzyme solution which loosens the ligaments or zonules. Small particles of lens material may be removed by irrigation. Once the posterior capsule has been removed, the phaco-emulsifier's work is done.

This technique has now been employed by Dr. Charles D. Kelman¹ on forty patients. The results were found to be fully as good as those removed by the old method except that it greatly reduces the patient's recovery time and post-operative complications. The old method of cataract extraction requires incision of 180 degrees requiring six to eight sutures, at least one week in the hospital, and four to six weeks recuperation at home. With the phaco-emulsifier technique, the patient can be out of bed a few hours after the operation with no restriction of activity after the first post-operative day.

In the first forty patients operated upon by Dr. Kelman, their vision two months to eighteen months after extraction was exactly the same as that ex-

pected with the standard surgical techniques. There were only minor complications and the appearance of the eye after three days is similar to that of eyes of six to eight weeks after standard surgical extraction.

The new technique has also been used successfully in three patients for removal of trauma induced hemorrhages with follow up of two months. If coagulated blood continues to block the outflow channels of the eye pressure is increased and glaucoma may develop. Furthermore, loss of vision is the usual result with such injuries to the eye. With the phaco-emulsifier, the clotted blood is emulsified and aspirated and vision restored.

With such a new technique one dreams of course of other possible uses of the instrument in other areas of the body. It could certainly be used in destroying and aspirating tumors. Then what about dissolving and aspirating gallstones, calculi and plaque filled arteries?

L.H.N.

Reference

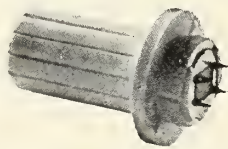
1. Kelman, C. D.: JAMA, 206: 1902, November 25, 1968.

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Management Of The Dying Patient: I.

All physicians are faced with the problem of management of the patient who must soon die.¹ These patients face loneliness, pain, suffering, the end of it all and are greatly in need of help and comfort. As for ourselves death requires looking at, if we can bear to do it. The fact is that actually we cannot do so if we but examine our own minds and those about us and also from an inspection of the medical literature. In 1906, Osler described the process of dying of 500 patients but thereafter there was little more in the literature for the next forty years. The last decade or two have produced a number of papers about death and dying but there is nevertheless a most remarkable scarcity when one weighs the importance and frequency of death compared to the triviality of some medical matters discussed frequently and at length.²

It may be asked do people die comfortably or miserably or at any rate as well as they might? Are we as wise in managing the universal condition of dying as we are clever in treating diabetes or heart failure? Can we reflect upon the man who died with comfort and dignity under our care with the same satisfaction we feel when we have cured pneumonia. There are several parts to the problem. One is concerned with the cultural background of the dying person. Another is the environment in which death takes place, the hospital, the street, the house. There will be the family, friends deeply or superficially involved. The character and age of the central actor in the play. Then there are the traditional comforters, the clergy who are thinking as much of the current necessities of the bereaved and less of the posthumous requirements of the deceased.

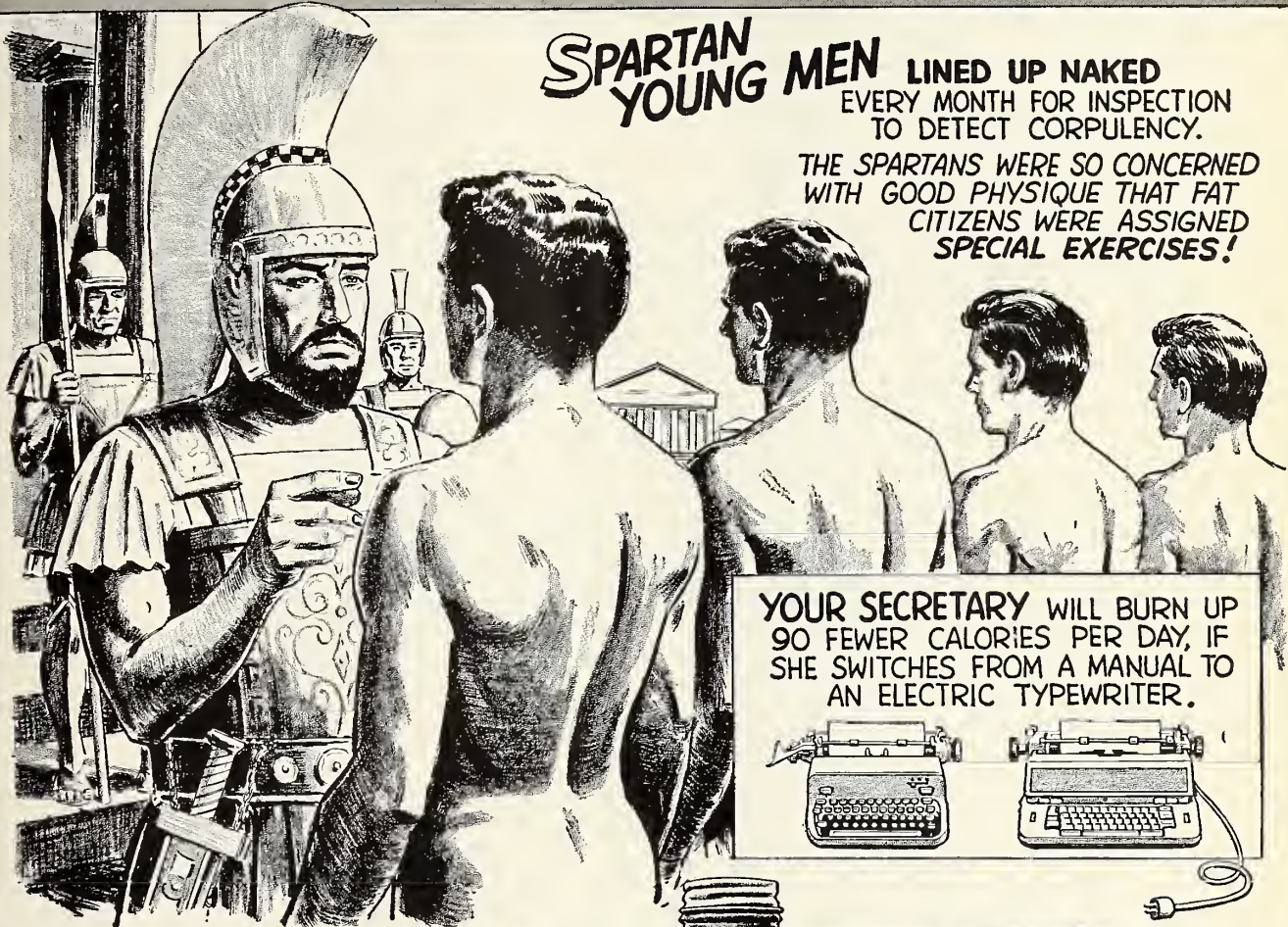
When presented with an intractable problem man uses a characteristic solution, magic, a variety of magical systems which have played a prominent part in thought and literature as far back as one can see. Magic is a limitless form of denial, but it is important to the physician to know the patient's particular system of belief to understand what is on his mind. If we know this we are less likely to project our own beliefs and anxieties onto the patient as though they were his. Furthermore, knowing this will help us to engender serenity in the patient.

Almost no one faces death in the same way and the doctor will need to modify his role in accordance with his patient's beliefs. Borkenau³ points out that many primitive societies act as though there was immortality. The dead may be painted or bodies

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FACT & LEGEND



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OVERWEIGHT PEOPLE ARE LEAST INTERESTED IN DIET IN DECEMBER.

JANUARY						
S	M	T	W	T	F	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

MAY						
S	M	T	W	T	F	S
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15	16	17	18	19	20	21
22	23	24	25	26	27	28
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JUNE						
S	M	T	W	T	F	S
1	2	3	4	5	6	7
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BRIEF SUMMARY/Indications: Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

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preserved. Their possessions and even their servants are entombed for their later use. Sacrifices are performed to propitiate them and the living try to "keep the dead alive" and to "keep them away." In early Egyptian society the Pharaoh was the only one certain of immortality and all others of extinction. Later the aristocracy contrived to improve their chances through mummification and later still the life everlasting became possible for all. Then followed a gradual loss of belief in direct immortality there arising instead the belief that there was a different and better world to be reached after death provided that one complied with certain ritualistic and magical rules while alive. Our own culture is in approximately this stage now.

Thus one's attitude is conditioned not only by the century of one's birth but also by the social status one has achieved or inherited. Most members of our society adhere to one of several systems of belief which proclaim death is not death at all but something quite different often associated with a system of rewards or punishment. In some places it is either illegal or improper to examine these contentions scientifically because society as a whole is involved in denial of death. Many people become very angry when their religious beliefs are discussed. The possible loss of security is too dangerous to be endured. Denial of death may be taken as far as to become preposterous. Jessica Mitford⁴ refers to medium priced metal caskets equipped with beauty-rama adjustable soft foam beds . . . as though the corpse will be more comfortable. This leads one to wonder whether there is indeed a general anxiety about death which is denied or whether people are not really concerned about it.

Alexander's study² of thirty-one Princeton undergraduates would indicate that there was something like the same amount of anxiety about death in a group of young men as about sex and school. Fulton⁵ revealed in his study of the American public that there were several significant differences among different groups. In one group of householders only one in five thought that death equalled the finish of life and everything else. In a more sophisticated group (club members) half took this view. Very few from either group thought that the funeral is primarily a religious event. Rather it is a way of comforting relatives and allowing one to pay his last respects. Another study by Diggory and Rothman⁷ of 563 non-random subjects revealed in general that those over age forty worry most over dependents. Those of the Roman Catholic faith worried most about the hereafter. The Jewish patients feared

first a painful death. In general it seemed that a person feared death because it eliminated opportunities to pursue goals important to his self-esteem. Thus the concepts of death vary widely. It is apparent that the doctor cannot manage his dying patient satisfactorily unless he takes due notice of this and does his best to appreciate the patient's own position.

In war and natural disasters the fear of death can be overwhelming and the usual mechanism of defense is denial not only among those at risk but also among those who are concerned with their problems. The military physician function seems to be not to analyze the repressive and reality denying psychological forces of denial, ritual and magic. They are his most potent allies. His task is to watch when they are about to fail and to take some sort of action. Here the doctor is deflected from his proper role by the harsh necessities over which he has no control and which he can but deplore.⁶

It is different in society. Probably more than a quarter of the population die in hospitals. Here because of the numerous personnel involved with each patient, there is danger of emotionally attenuated treatment. The nurse spends the most time with the patient, attends to his bodily comfort. The patient looks to them also for emotional comfort, but the nurse is usually uninformed about the patient's illness and what it means to him and how to talk to the patient and give him comfort. In many hospitals with their orientation toward research and training, the patient's comfort may at times be jeopardized rather than enhanced.

Another important concern of the physician is the kind of family the patient comes from. If he comes from a large interdependent mutually supportive family then each member is less vulnerable to the loss of another member. In such a family the general pattern of life will go on. The dying man knows his children will be brought up in a relatively stable family circle. There are also possible frictions in a large family structure but the best features seem to come out under circumstances of threatened death. In the smaller family there are problems. The marital couple may not share their friends, their entertainment or their lives. They may have separate relationships. In case of impending death or bereavement support may be missing. The doctor responsible for the situation must have some notion of what is going on if he is to intervene usefully. For both of the principles may have been leading quite isolated lives with few or no relationships of any significance to them. So that as death approaches



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As the "middle years" exact their metabolic toll, complaints are vague, but therapy can be specific.

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isolation of the living may become more marked. The doctor must help to uncover the reserves of love, concern and tenderness of which they are in such great need.

The segregation of the dying is well established in many cultures and if anything is becoming more marked in ours as a general pattern of dealing with the aged. Nothing destroys an old person so quickly as the removal of familiar things, places and relationships. In some institutions there is a general tendency for the dying and the aged to be left alone before they are dead. Sometimes the relatives deal with their own anxiety by moving out and sometimes the dying person is being paid back for years of rejection and domination of those who might have comforted him now. It is not wise to judge hastily and not allow anxiety about one's own death to lead to condemnation of the absent comforters.

There are many things to be said about the effect of death on the surviving members of the family, since no one really knows what "normal" bereavement is.

L.H.N.

References

1. Ellard, J.: Emotional reactions associated with death. *Med. Jr. Austr.*, 1: 979, June 8, 1968.
2. Alexander, I. E.: Is death a matter of indifference. *J. Psychol.*, 43: 277, 1957.
3. Borkenau, F.: The concept of death. *The Twentieth Century*, April 1955.
4. Milford, J.: *The American way of death*. Penquin Books, Middlesex, 1965.
5. Fulton, R.: The sacred and the secular attitudes of the American public towards death. Reprinted in *Death and Identity*, Wiley, New York, 1965.
6. Grinker, R. R. and Spiegel, J. P.: *Men under stress*. Blakiston, Phila., 1965.
7. Diggory, J. C. and Rothman, D. Z.: Values destroyed by death. *J. Abnorm. Social. Psychology*, 63: 205, 1961.

The Role Of Proteins In Membrane Transport

Living cells need membranes to hold their contents together, to keep metabolites from diffusing away and to keep out toxic materials. But the membrane also constitutes a barrier to nutrients being brought in and waste products being excreted. And so we find transport systems built into membranes in a way that provides selective permeability. By this process only the necessary materials are transported. In some cases transport systems do more, they actually "pump" substrates to create a higher

concentration inside the cell than outside. This requires energy and is termed active transport to distinguish it from facilitated diffusion which does not require energy and is called passive transport. Substances like Na. ions are pumped out from animal cells.

If transport systems exist what is their structure, how do they work and what chemical machinery is required for the specific translocation of small molecules from one side of the membrane to the other? Much of what we know about this has been learned in the last several years. The problem is biochemical and the approach to its solution is analysis followed by synthesis. First the parts and their properties need study. Then from this information plus observation on the intact system one proceeds to devise a plausible model of how the complete system works. Eventually the hope is to put the parts together physically and reconstitute the entire operating system. The trouble with applying such an approach to transport is that once one takes cells apart transport can no longer be measured. This is why for many years there seemed no way of determining whether any isolated molecule was or was not part of the transport system.

All models assume that the first step is a specific binding of the substrate to an active site on the outer membrane surface much as a substrate is bound to an enzyme. There then follows translocation of the substrate across the membrane, a process whose details are completely mysterious. The substrate must then be released inside the cell and then the system returns to the original state. If the transport is active it must supply energy at one of these steps so that inflow is more effective than outflow. For example one system transports glucose and the closely related sugars 3-0-methyl glucose and 2-deoxyglucose into animal's cells while other sugars are excluded. The initial rate of entry would depend on its concentration as though there were a limited number of independent absorption sites. Another method is for one substrate to stimulate the flow of a similar substrate in the opposite direction as though the two processes shared a component of the system such as a carrier molecule in the membrane that cycles between inward and outward sites. If energy is needed for active transport then compounds which inhibit energy cell production should inhibit active transport and they do.¹

Proteins in the membrane probably constitute the recognition sites because they have the specificity to discriminate between possible substrates. Also inhibitors of protein synthesis such as chlorampheni-

col prevent synthesis of transport systems in bacterial walls. The question is then whether these proteins can be isolated. One expects transport proteins to be located on or near the cell membrane. Actually Electron-microscope photographs show that the membranes are three-layered structures about 70 angstroms thick and isolated membranes do consist of 60 per cent proteins and 40 per cent phospholipids. It also appears likely that there is a protein-lipid mosaic¹ and the proteins might extend through the membrane in some places providing specific doors for transport processes.

Several proteins have now been isolated through differential labeling. One for sulphate binding in salmonella typhimurium. One that binds calcium has been isolated from several tissues of chicks and rats. A protein from escherichia coli binds neutral amino acids. One that binds galactose one that binds glucose, another glucose-6-phosphate and L-arabinose. These proteins are all similar but not identical with molecular weights around 30,000. There are also energy-coupling proteins. One such has been related to the bacterial transport of nine sugars and is released inside the cell as a phosphate derivative, catalyzed by a specific enzyme. Thus there appears to be a specific enzyme for sugar and the enzymes are bound to the cell membrane. The energy supply for Na. + K. is ATP, which phosphorylates a group of membrane proteins. These are large lipoprotein molecules (weight 670,000). Affinity sites for the substrates Na. and K. as well as for the energy donor ATP, have been found.

Location of transport proteins are probably on or near the membrane. The unique step in their function is movement of the substrate across the membrane. Two general mechanisms to achieve this have been suggested. In one, the "recognition" protein is an enzyme that catalyzes bond-formation between substrate and a low molecular weight transporter in the membrane. The second hypothesis holds that the recognition protein itself carries the substrate across the membrane and a variety of detailed mechanisms have been suggested for the translocation process. For example part of a protein can be exposed to either the exterior or interior of the membrane. At least one, the sulphate binding protein is actually long enough to stretch across the membrane.

Thus we see that isolation of these proteins answers one question about transport system showing where the specificity of recognition resides and rapid progress is being made in discovering the way in which energy is linked to transport. Nature seems to

have devised several different mechanisms for active transport. In some cases the energy source reacts with the substrate while in others it reacts with proteins of the membrane system.

Transport systems cannot have many specific parts because few genes are involved in any of them. This fact gives promise of our soon understanding transport to a degree that we now understand enzyme catalysts.

L.H.N.

Reference

1. Pardee, A. B.: Membrane transport. *Science*, 162: 632, November 8, 1968.

Purified Influenza Virus Vaccine

The development of procedures for the use of the K.-11 continuous flow zonal ultracentrifuge has resulted for the first time in the availability of large quantities of highly purified influenza virus vaccine essentially free of non-viral egg-derived material. This represents a major technological advance. The preparations are consistently free of side effects in all population groups studied regardless of age or occupation. This means that the great majority of side effects produced by conventional vaccines were not due to inherent viral toxicity.

With highly purified virus preparations, there was no basic difference in the inherent reactogenicity of individual virus strains or combinations thereof. Furthermore, it became evident that the non-viral components of conventional vaccines do not increase antigenicity by acting as adjuvants. The ability of purified vaccines to be administered at twice the usual potency level without an increase in symptoms indicates that the way is now clear for additional studies on the use of experimental vaccines of even greater antigenic mass.

It should now be possible to determine the most effective level of influenza virus consistent with a low incidence of local constitutional reactivity. The purified vaccines used by Peck¹ in his report in the *JAMA* are essentially free of demonstrable avian antigens, and it is reasonable to predict that anaphylactic or other allergic reactions due to the sensitivity of the individual to avian antigens will be materially reduced if not entirely eliminated. Only time will tell.

During the 1967 to 1968 influenza season a purified bivalent influenza virus vaccine was distributed for general field use. To date there were no reports

A high index of suspicion... E. coli

How high is the "index of suspicion" for *E. coli* in urinary tract infections?

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Gantanol also earns its high "index of confidence" because Gantanol therapy is relatively free from complications, including the problem of bacterial resistance or superinfection.

Convenient, economical dosage schedule: *b.i.d.*

References: 1. Vernier, R. L., in Patient Care Feature: *Patient Care*, 1:20 (Feb.) 1967. 2. Beeson, P. B.: "The Infectious Diseases," in Beeson, P. B., and McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Philadelphia, W. B. Saunders Company, 1967, p. 230.

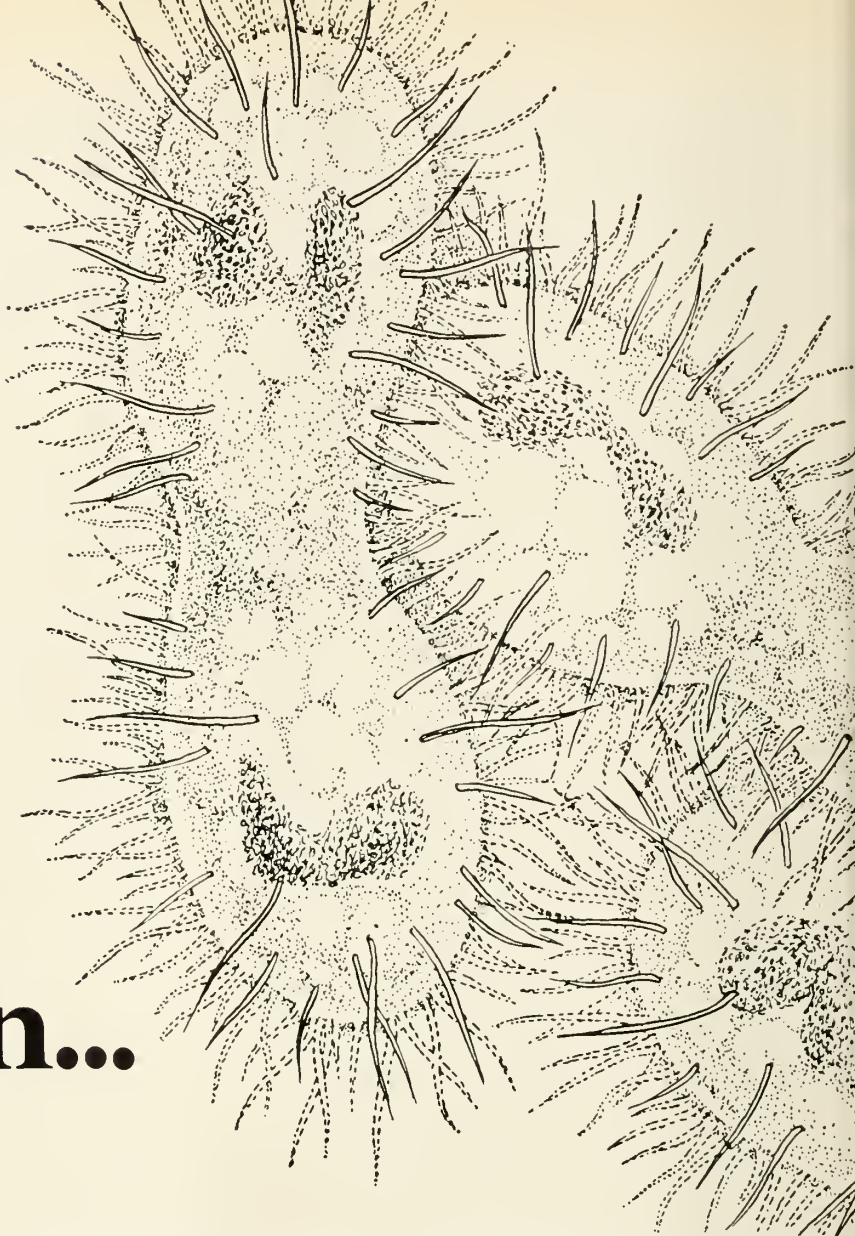
Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute and chronic urinary tract, respiratory and soft tis-

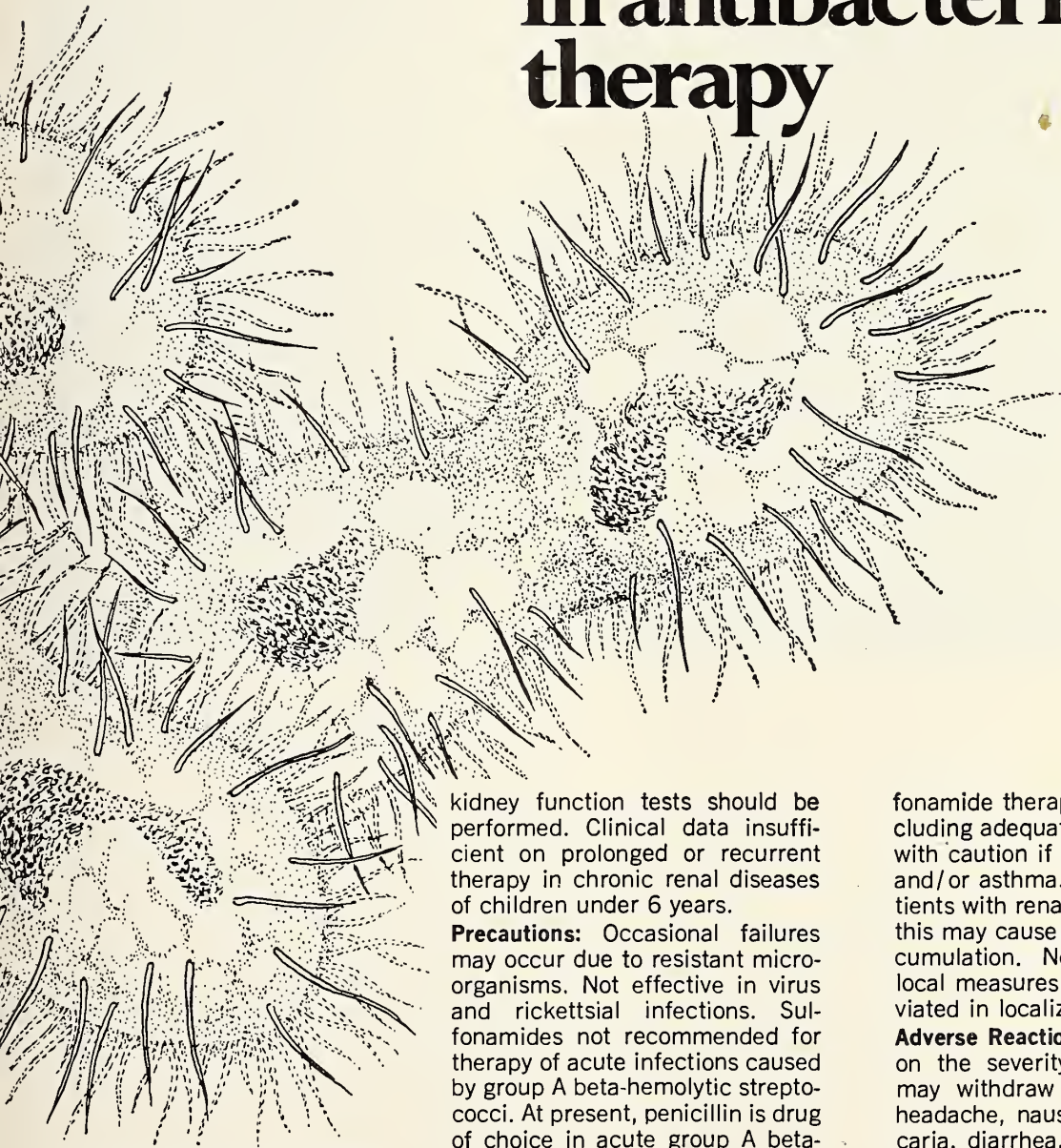
sue infections due to susceptible microorganisms; prophylactically following diagnostic instrumental procedures on genitourinary tract.

Contraindicated in sulfonamide-sensitive patients, pregnant females at term, premature infants, or newborn infants during first 3 months of life.

Warnings: Use only after critical appraisal in patients with liver or renal damage, urinary obstruction or blood dyscrasias. Deaths reported from hypersensitivity reactions, Stevens-Johnson syndrome, agranulocytosis, aplastic anemia and other blood dyscrasias. In closely intermittent or prolonged therapy, blood counts and liver and



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Artist's rendition of *E. coli*. As with most strains of *E. coli*, these have flagella and are motile.

kidney function tests should be performed. Clinical data insufficient on prolonged or recurrent therapy in chronic renal diseases of children under 6 years.

Precautions: Occasional failures may occur due to resistant microorganisms. Not effective in virus and rickettsial infections. Sulfonamides not recommended for therapy of acute infections caused by group A beta-hemolytic streptococci. At present, penicillin is drug of choice in acute group A beta-hemolytic streptococcal infections; although Gantanol has produced favorable bacteriologic conversion rates in this infection, data insufficient on long-term follow-up studies as to its effect on sequelae of rheumatic fever or acute glomerulonephritis. If other treatment cannot be used and Gantanol is employed in such infections, *important that therapy be continued in usual recommended dosage for at least 10 days*. Observe usual sul-

fonamide therapy precautions, including adequate fluid intake. Use with caution if history of allergies and/or asthma. Follow closely patients with renal impairment since this may cause excessive drug accumulation. Need for indicated local measures or surgery not obviated in localized infections.

Adverse Reactions: Depending upon the severity of the reaction, may withdraw drug in event of headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, Stevens-Johnson syndrome, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.



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of allergenic reactions and instances of severe local inflammation or febrile episodes following its use have been reported at a rate of less than 1 per 100,000 doses distributed. This certainly is good indirect evidence that zonal centrifuged vaccine offers a means of immunization against influenza with a very low incidence of side effects.

The introduction of this new purified vaccine has exposed some of the erroneous notions we entertained about the old vaccine. The reactivity of impure influenza vaccine had been attributed to two main causes. One notion was that since influenza is a myxovirus that it is inherently toxic and capable of producing constitutional symptoms such as malaise, chills and fever as well as local inflammation at the site of injection of the vaccine. The purified vaccine has disproved this view. Then there was speculation that since the vaccine virus was grown in embryonated eggs perhaps the egg fluids and their non-viral components were responsible for the major reactivity of the vaccine. The production of the purified vaccine has confirmed the second view that the reactivity of the old vaccine actually can be attributed to the non-viral components of conventional vaccine and that this reaction had nothing to do with the production of immunity.

Formerly we gave only fractional doses of vaccine or none at all to old and debilitated individuals who are at increased risk due to their infirmities for fear of local or constitutional reaction. The new vaccine can be given in full or even doubled strength doses without reactions of any kind.

L.H.N.

Reference

1. Peck, Jr., F. B.: Purified influenza virus vaccine. *JAMA*, 26: 2277, December 2, 1968.

Some Recent Events Of Special Interest In Medical Education: I. Manpower Activities

Many new things are happening in medical education. Major attention is being given to health manpower problems especially the need for more physicians, the financial plight of medical schools, the increased opportunities for medical education of the poor, increased student activism and student interest in curricular affairs. Not the least of these is the major efforts by most medical schools to effect significant revisions in their teaching programs.

Public and professional concern for the status of

the supply of health manpower has led to a variety of conferences, studies and reports on this subject which dominated the scene in 1968. The recommendations of President Johnson's National Advisory Commission on Health Manpower had particular implications for medical education. It urged the production of a sufficient number of physicians to meet this countries needs and further to assist other countries particularly developing nations to improve their systems of medical education and their levels of medical practice and public health. It urged production of physicians beyond presently planned levels by a substantial expansion in the capacity of existing medical schools and by development of new schools. This would require federal funds in support of capital or operating costs of education in such a way that they create economic incentives for the school to expand its enrollment at the same time improving its quality.

The federal government is asked to carefully explore ways to provide support directly for the educational function of the medical school and to make available loans to any medical student to cover the full cost of tuition and living expenses during the formal professional education. The government is asked to markedly expand support for research in the educational process for physicians and other health personnel. Finally it is urged that professional societies and state governments should explore the possibility of periodic relicensing of physicians and other health professionals. Relicensing to be granted either upon certification of acceptable performance in continuing education programs or upon the basis of challenge examinations in the practitioner's specialty.

On March 5, 1968 both the AMA and the AAMC endorsed the position that all medical schools should now accept as a goal the expansion of their collective enrollments to a level that permits all "qualified" applicants to be admitted. The number of rejected applicants is about 9,000. Even if they were all "qualified" that is capable of completing medical studies successfully and possessing other characteristics of physicians acceptable to society, there would not be room for all even though new medical schools are being established at an unprecedented rate and most existing medical schools expanded their enrollment to the limit.

The joint statement of the two groups also stressed the need for curricular innovation which would shorten the length of the training period and open alternate pathways to the M.D. degree. Clearly implementation of these measures would require ade-

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quate financial support from government and private sources for construction and operation of schools and for experimentation in educational innovation. Each medical school was asked to re-examine its objectives, educational programs and resources to determine how it might contribute most effectively to meeting the national goals.

In 1968 a number of federal laws of importance to medical education expired and a new Health Manpower Act, Public Law 90-490 was passed August 17, 1968. The act provides for construction grants and grants depending on student enrollment as well as number of graduate students per year. In awarding the grants priority is to be given to the extent to which the project will increase enrollment, the relative need and the extent to which the project will result in curricular improvement and shortening of the training period provided it does not adversely affect the quality. In exceptional circumstances the grant could be for as much as a million dollars.

The National Academy of Sciences has also entered the picture in 1967 by establishing a Board of Medicine which it is hoped will become a new national policy making body in the field of medicine. The Board immediately launched a study of Biomedical Education for the future. There is also a University Hospital Program cost study which may well provide the first sound basis for revision of many long established attitudes relating to proper apportionment of interne and resident expenses to the different hospital programs.

In the last year or two a marked increase occurred in student unrest in American universities. Issues such as war and peace, poverty and race relations typically attracted student concern. Medical students role in the past was a relatively passive one, not concerning themselves with problems of the society surrounding them. It seemed usually to have been accepted that the role of the faculty was to teach and of the student to learn. If there was any student criticism it was directed to periodic criticism of individual courses or instructors. This passive role of the medical student seems to be disappearing rapidly.

The activism of the medical student has not taken on any violent form. They had and seized the opportunity to become involved with the ills of society at large and the problems related to the organization and delivery of medical care. They have during the summer vacations and during the school year organized and participated in various programs in efforts to improve the health care of

the less fortunate. Within the medical schools they have sought a greater voice in the organization of the curriculum and examination and promotion of procedures and quality of teaching. Their interest in the curriculum is focused particularly in such areas as community medicine and delivery of health care because this bears particularly in such areas on the social ills of today's society and to which they feel medical schools have not devoted proper attention in the past. From this we may infer that medical students are going to seek to play a more active role in their own education than in the past.

The negro and Puerto Ricans are a segment of the population which is grossly under represented both in medical practice and in medical school enrollment. Accordingly many medical schools now are actively searching for qualified negro applicants, but no significant increase in the number of negro applicants to medical schools has occurred in the last twenty years. For this reason it is important that active steps be taken to prepare a greater number of negro students for careers in medicine. This means that genuine solutions must emanate through improved curriculum, better teaching and specialized courses of training at all school levels for promising negro students. Special college courses, additional scholarships and summer programs for special study for students about to enter medical schools. We will need special projects for negro high school students such as are now being sponsored by members of medical school faculties as well as better guidance and counselling programs in high school and colleges. A number of national organizations and institutions are now concerning themselves with this problem.

The medical schools, however, can only accept students capable of coping with the medical courses. As medical schools develop curricula that are less rigid and make provisions for students to progress to the M.D. degree at different rates, it will become possible to train more negro physicians who are medically competent. These developments together with adequate counselling offers hope that students who have the potentialities desired in a physician may overcome deficiencies in their preparation and take their proper place in medicine.

L.H.N.

Reference

1. Medical education in the United States. JAMA, 206: 1988, November 25, 1968.

Medical Aspects Of Driver Licensing

Motor vehicle crashes took the lives of 53,000 persons in 1967 and caused more than 1,900,000 disabling injuries.^{1, 3} Add to these figures milder injuries and there were probably over 6,000,000. Unless this picture changes radically one person out of every eight in the U.S. will be killed or injured by a motor vehicle within the next four years. This eventuality constitutes one of the nation's largest unsolved health problems and we physicians must face the challenge. We must recognize physical and mental disorders likely to impair driving ability and also recognize problems resulting for medications and alcohol.²

The AMA's Committee on Medical Aspects of Automotive Safety has produced a "Physician's Guide for Determining Driver Limitations" to help us determine if driver limitations exists.⁴ Does the individual lack the physical and mental ability to manipulate controls? Does the patient fail to meet specific vision and hearing standards? Is he likely to suffer excessive fatigue? Does he have disorders likely to cause loss of consciousness or other impairment of driving ability including antisocial behavior or an emotional disturbance? Is he likely to suffer a temporary impairment due to alcohol, drugs, infectious or medical treatment which make it unsafe for him to drive?

Because of the confidentiality of medical records and the professional nature of the physician-patient relationship, generally physicians will not report a patient's condition to licensing authorities unless required to do so by law. Nevertheless the physician should use all his influence to urge the patient who has a condition that would make him an unsafe driver to refrain voluntarily from driving if the condition is temporary. If the condition is likely to be permanent then the patient should be urged to surrender his license.

The physical and mental demands of the task of driving vary greatly with the type of vehicle and the type of driving. The driver of the private vehicle in many cases may select both the time of his travel and the route. The driver of the commercial or passenger transport vehicle usually cannot choose the hours he will drive nor the route he will take. Drivers of such vehicles also usually spend more hours driving than do most drivers of private vehicles. The physician should bear in mind that there is little similarity between the demands on the individual who drives but a few miles a day in an area of little traffic and the in-

dividual who drives in rush-hour traffic in a metropolitan area.

The operation of modern high-speed motor vehicles requires split-second reaction by the driver. There seems little doubt that poor judgments, drinking, faulty attitudes, emotional disturbances and physical disabilities including impairment of the sensory organs are basically responsible for many crashes. It is the driver who is the key to cutting down the accident toll, his intelligence, sense of personal and social responsibility, his reactions to various stimuli in both normal conditions and under stress, his driving ability in good health and in illness.

We physicians are trained to ascertain the physical or mental impairment of an individual and so are in a good position to evaluate the impairment in relation to safe-driving ability. It is not always easy to arrive at a decision in such cases because individuals vary in response to drugs, in severity of illness and impairment from time to time. Nevertheless, in the realm of behavior patterns we can do effective counselling. Patients must be made to realize that alcohol is involved in over 50 per cent of all fatal crashes. We need to impress upon the patient that even a small amount of alcohol can interfere with a driver's thinking to the point that he does not realize that he is materially increasing his likelihood of serious injury or death.

A patient with a specific health problem usually has a receptive attitude towards his physician's advice. The physician in turn carries a responsibility to protect the safety of his patient and should caution his patient when necessary against driving for a certain period of time or even permanently. He can refer the patient to the AMA pamphlet "Are You Fit To Drive" which describes for lay readers conditions under which one should not drive. While it is true that physicians do not issue or remove licenses, they do carry a responsibility to the patient to identify for him medical factors that would threaten his safety, his life and that of others if he should drive.

Problems relating to medical factors and driving ability will become more and more prevalent. Doubtless medical review boards will be set up in every state to arbitrate situations in which there is disagreement about the patient's ability to meet specified physical and mental standards. Such review boards can also offer guidance to state licensing agencies in the establishment of such standards. Such boards are described in "Medical Advisory Boards for Driver Licensing" published by the

AMA in conjunction with the American Association of Motor Vehicle Administrators and the U.S. Public Health Service.

On the local level physicians can help to improve licensing procedures of county and city licensing personnel. For this purpose a recently published AMA guide "Determination of Need for Medical Evaluation in Driver Licensing" is now available to assist authorities in determining which applicants for driver's licenses require medical examination. The physician's major role is to help to prevent motor vehicle crashes through appropriate advice and treatment of patients. At the same time they should be interested also in preventing or reducing crash injury.

The elimination of many road hazards is proceeding and there is continuing pressure for improvement in the safe design of vehicles and more will be done in these respects since it is not too difficult to change mechanical things. The big difficulty is to change man's behavior. The public will have to be educated to pay for the mechanical changes, learn to use seat belts and shoulder harnesses.

Looking ahead there will probably be more stringent standards for driver licensing and many more drivers will require medical evaluation than do now. Inevitably we as physicians will become more involved in the problem. The AMA Committee on Medical Aspects of Automotive Safety has the pamphlets to assist the physician. Any specific problem not covered in the guides should be addressed to this committee who stand ready to answer them.

L.H.N.

References

1. Accident facts—1967 Edition, Chicago National Safety Council, 1967, p. 2.
2. The role of the physician in driver licensing. JAMA, 206: 2305, December 2, 1968.
3. Miller, H. G.: Traffic safety holds the line in 1967. Traffic Safety, 68: 12, 1968.
4. Proceedings House of Delegates. American Medical Association, November 26-30, 1967.

The Effects Of Carbon Monoxide On Human Health

Exposures to carbon monoxide (CO.) are widespread. For the U.S. urban population cigarette smoking is probably the most important source followed by motor vehicle exhaust, occupational sources, home heating, and cooking devices. It is generated by incomplete combustion. In New York city alone each day auto traffic produces 8.3 million pounds of CO. Each car emits 1/6 pound per mile

of travel at 25 m.p.h. and 1/3 pound at 10 m.p.h. In Los Angeles 20 million pounds of CO. were emitted by motor vehicles during 1967.¹ The peaks occur in urban areas dependent on the automobile for commuting in the morning, but in downtown New York the peak is day-long. The exhaust control devices now in use have reduced CO. emission, but this is offset by the fact that as vehicles grow older the effectiveness diminishes. More older vehicles will be on the road and their number will greatly increase by 1980. All this will vitiate the value of exhaust control devices.

CO. occurs in high concentration in cigarette smoke greater than 2 per cent, this means 20,000 ppm. although an estimate of the average concentration in smoke is much less—400 ppm. In a population of longshoremen smoking produced 6 per cent of COHb. When it comes to occupational exposure 12-14 per cent of employed persons had occupations in which there is a likelihood of exposure. Various forms of indoor combustion may emit CO. and a number of deaths each year are due to poisoning from this source. Gas fired baseboard heaters were incriminated by Michigan State Department of Public Health. Open fires and charcoal braziers produce substantial amounts of CO.

The major effect of CO. is to impair oxygen transport by the blood through two distinct mechanism. We should recall that CO. affinity for Hb. is 210 times greater than for O₂. Thus a small quantity can reversibly inactivate a substantial percentage of O₂ carrying capacity of the blood. Even small quantities of CO will progressively accumulate in the body by virtue of its strong affinity for Hb. The second effect is to interfere with release of O₂ carried by the Hb. molecule at the tissue level where O₂ is decreased by 40 per cent of saturation. This substantially decreases O₂ liberation and increases the hazard of CO. toxicity at high CO. concentrations.

Since the effect of CO. is an impairment of O₂ transport to the tissues, at high altitudes, at other situations where O₂ tension is low as in anemia and vascular insufficiency especially in brain and heart the effect of a given concentration of CO. will be correspondingly more severe. Thus the population group that is most susceptible to the adverse effects of atmospheric CO. includes persons with severe anemia or impairment of circulation to vital organs of the body. In such individuals community exposure which produce 5 per cent concentration of COHb added to the burden of an

unfavorable occupation and especially of cigarette smoking exposures could greatly increase morbidity and also mortality rates. It is obviously the better part of discretion to reduce community and occupational exposure to a safe level below 20 ppm. and to prevent smoking at work and during driving in traffic.

We now have in addition three important facts about CO. One is that it is produced endogenously from metabolism of heme. The other is a clearer definition of the effects of CO. on selected functions of the nervous system. The third is improvement in methods for epidemiologic study of possible effects of CO.

Endogenous CO. which is produced at the rate of .5 to 1 ml. per hour increases in patients with hemolytic anemia, extensive trauma, following certain surgical procedures and transfusion reactions. Accordingly we must be on the alert for CO. excess in patients undergoing anesthesia. Closed rebreathing systems are now opened and flushed periodically during operative procedures to remove the excess of CO. Endogenous production of CO. in newborn infants especially those with abnormal hemolysis has produced COHb. concentrations as high as 12 per cent implying markedly impaired oxygen transport.

Production of CO. was also noted in other closed systems that contained men as for example submarines in which CO. arises from internal combustion engines, tobacco smoke and exogenous sources. The accumulation of CO. would appear to be hazardous unless attention were turned towards endogenous production of CO. in closed systems being developed for use in space flights as well as undersea explorations. In a recent experiment four men were confined for a fourteen day period in a closed system having a volume of twenty-eight cubic meters. At the end the CO. concentration had increased to 19 ppm.

It is conceivable that the animal-plant cycles proposed for use in long space flights to produce O₂ and remove waste products will themselves be a source of CO. as a result of the decomposition of chlorophyll which contains a cyclic tetrapyrrole similar to heme. In fact mature leaves have been shown to produce large quantities of CO. presumably from degradation of this pigment.

The fate of atmospheric CO. is not entirely known but it has been suggested that a true CO. cycle exists in nature since it can be produced by plants and by many lower animal species, can be utilized for metabolic purposes in certain bacteria

and plants and may be oxidized to CO₂. at slow rates in animals and man.

CO. in concentrations of 5 per cent has a definite effect on visual threshold. Healthy subjects exposed for 90 minutes to CO. in concentrations as low as 50 ppm. show reduced ability to perceive differences in the duration of auditory stimuli and develop some hearing impairment. Similar levels of CO. commonly occurring in heavy traffic could therefore adversely influence vehicular operations. Smokers while driving are inhaling at least 400 ppm. CO. and certainly should be suspect as far as ability to drive safely since their acuity of vision and reaction time is definitely impaired.

Grut² alleged that 46 per cent of 721 drivers had chronic CO. poisoning characterized by fatigue, headache, irritability, dizziness, disturbed sleep and other symptoms. Some subjects had abnormal neurological symptoms. From the epidemiological point of view it is desirable to obtain data which would show whether there are CO. associated increases in such relatively frequent events as motor vehicle accidents or in fatality rates with myocardial infarction to confirm the data from the Los Angeles Hospitals where an association of CO. and case fatality rates in 3,080 patients with myocardial infarction was observed. The central nervous system effects are definitely due to anoxia. The mechanism of myocardial effects probably are similarly produced. Lindenberg³ did obtain significant electrocardiographic changes on exposing dogs for six weeks to 50 ppm. CO. They also showed dilatation of the right ventricle, scarring of heart muscle and fatty degeneration. A very important question for epidemiologists to study is whether exposure to low concentrations of CO. have a role in the development of human heart disease. Inferring from results of acute toxicologic and experimental studies, we can begin to appreciate the abundant data linking cigarette smoking to coronary heart disease. As far as cigarette smoking is concerned we must keep in mind that high levels of COHb. imply also increased respiratory absorption of other ingredients of tobacco smoke.⁴

It is safe to say that exposure to CO. is widespread, that the smoker who inhales 6 per cent CO. is developing a blood concentration which is a serious threat to the health in persons with underlying cardiovascular disease. It is also true that community air pollution may produce COHb. in non-smokers similar to that observed in smokers. Even low and commonly occurring CO. exposures may impair performance of complex psychomotor tasks.

Finally that CO. has a role in motor vehicle accidents, is supported by data of high COHb. in many drivers involved in accidents.

L.H.N.

References

1. Goldsmith, J. R. and Landow, S. A.: Carbon monoxide and human health. *Science*, 162: 1352, December 20, 1968.
2. Grut, A.: Chronic carbon monoxide poisoning. (Munksgaard) Copenhagen, 1949. p. 44.
3. Lindenberg, R., Levy, D., Preziosi, T. and Christensen, M.: paper presented at a meeting of the American Industrial Hygiene Association, Washington, D.C., 1962.
4. Nahum, L. H.: Toxic products in cigarette smoke: pleasure or poison. *Conn. Med.*, 32: 154, March, 1968.

Exercise And Coronary Heart Disease

The relationship between physical activity and coronary heart disease has been the subject of numerous investigations, and many physicians are advocating year-round regular exercise to lessen the risk of heart attack.

Epidemiological Studies

In one of the earliest occupational studies, J. N. Morris et al. (*Lancet*, 2:1053, 1953) reported that the frequency of coronary heart disease in London bus conductors was about 30 per cent lower than in the less active bus drivers. An inverse relationship between the incidence coronary heart disease and physical activity has also been reported by many other investigators; major epidemiological studies in the United States include the Framingham Study (W. B. Kannel, Public Health Service Publication No. 1515, Washington, 1966), and the Health Insurance Plan of New York Study (C. W. Frank et al., *Circulation*, 34:1022, 1966). These studies took into account both work and play in rating physical activity. On the negative side, no relationship between coronary disease and occupational activity was found in Los Angeles civil service employees (J. M. Chapman et al., *Amer. J. Public Health*, 47:33, 1957), or in employees of the Peoples Gas Light and Coke Company in Chicago (J. Stamler et al., *Arch. Environ. Health*, 13:322, 1966; and Progress Report to the National Heart Institute, 1968).

Pathology Findings

In a cooperative study involving 206 hospitals in England, J. N. Morris and M. D. Crawford (*Brit. Med. J.*, 2:1485, 1958) correlated gross post-mortem findings with the previous job classifications of about 5000 men aged from 45 to 70 years, regardless of the cause of death. Although atheromatous changes in the coronary arteries of active and sedentary men were similar, large healed infarcts and focal myocardial fibrosis were much more com-

mon in those who had done light physical work than in those who had done heavy work. In post-mortem studies of 207 "normal" men who had died suddenly from accident, homicide, or suicide, D. M. Spain and V. A. Bradess (*Circulation*, 22:239, 1960) also found no significant differences in the degree of coronary atherosclerosis in sedentary and physically active men; however, the study provides no data on the incidence of healed infarcts or focal myocardial fibrosis.

Physical Training Programs

Generally, the aim of physical conditioning programs for patients with coronary artery disease has been to make the exercise strenuous enough to enhance the development of collateral circulation, but not so strenuous as to invite attacks of coronary insufficiency. In one of the largest studies in which exercise programs were prescribed (H. K. Hellerstein et al. in A. N. Brest and J. H. Moyer, *Atherosclerotic Vascular Disease*, New York: Appleton, 1967, p. 115), 189 of 485 subjects had previously suffered myocardial infarcts or had been subject to attacks of angina. The death rate in the 189 subjects during a follow-up period averaging two years is described as being much lower than the corresponding general death rate in patients who had suffered a first infarction and who had not had the benefit of conditioning programs. The study tells little about the effects of exercise alone, however, since the conditioning program included, in addition to exercise, reduction of fat in the diet, attainment of normal body weight, abstinence from the use of tobacco, and continuation of gainful employment and of a normal social mode of life.

Conclusion

It has not yet been definitely established that regular exercise by itself significantly reduces the incidence or severity of coronary disease. However, many Medical Letter consultants and other clinicians believe that present evidence justifies the physician in recommending exercise or sports programs suited to the patient's physical and psychological needs and limitations. They believe that such programs should be continued throughout adult life. Exercise should be combined with other measures such as reduction or elimination of cigarette smoking, weight reduction in obese patients, and diets low in cholesterol and saturated fats. In patients with hyperlipidemia which cannot be controlled by diet, and use of clofibrate (Atromid-S) may be advisable (*Medical Letter*, Vol. 9, 45, 1967).

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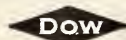
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THE PRESIDENT'S PAGE

Just before Thanksgiving I was asked to speak at the dedication of an addition to the Griffin Memorial Hospital in Derby. The people in the audience looked so proud of their new facility that I was more than pleased to play a part in the observance. Prior inquiry had told me a great deal about the hospital, past, present and future. I was impressed by what I found out.

The fact that interested me most was the amount of money contributed by the employees of the hospital. To me, this was clear evidence of the esteem in which the hospital was held. It also demonstrated that those close to the situation realized the need for more and better facilities for the care of the sick in the community. Too, it became apparent to me that although large gifts are a necessity in such a project, it is important that there are many small sacrificial gifts made by people who thus indicate an abiding interest and faith in their community.

Surely this fine new hospital is a memorial to all those who gave so generously to make the addition possible. And yet we must all realize that as a memorial this hospital goes back much farther than the present givers. Indeed, this is a memorial to all those people who have made this hospital possible from its very beginning. Yes, it is merely an expansion of their vision and initiative. Each brick that is added enlarges the memorial that much more. I was pleased to notice a plaque on the wall of the new structure declaring that it was a memorial to those who had taken part in the construction of the hospital from its beginning up to the present day.

In much the same way, the medical care now being enjoyed by the people of this country is a memorial to all the doctors who have gone before us. They have built the knowledge of disease and its treatment bit by bit, being sure to share with all doctors the learning acquired by each. Thanks to all this we have the finest medical care the world has ever known. Doctors, you and I are part of this heritage. Let us each resolve to add our own bit to this memorial.

NORMAN H. GARDNER, M.D.

Foreword

That this country can successfully send men to the moon and back while in the throes of a nationwide epidemic of influenza about which it can do virtually nothing, is the height of scientific irony, yet it is typical of the many incongruities which exist today in the fields of medical science and public health. From the early days of Connecticut's pioneer in public health, Dr. Charles-E. A. Winslow, to the present, the advances in medical knowledge have far outstripped the systems presently operative for its application.

In trying to catch up with the knowledge explosion a better understanding is required than most of us have of the various circumstances in which medical capabilities may be applied. For this reason, in selecting topics for inclusion in an issue of *Connecticut Medicine* devoted to Public Health, a deliberate effort was made to touch on widely differing approaches to just a few of the many types of health problems which our society faces. At the same time it is not the intention to present material which anyone believes Connecticut physicians "ought" to know, but rather to present that which they have, through numerous inquiries, expressed a real "desire" and day-to-day "need" to know.

The author of each of these papers has, in his own way, had considerable experience with the particular aspect of Public Health and Community Medicine which he presents, and it is hoped that the sharing of these varied professional interests, experiences, and plans will help to close the present gap which exists between medical knowledge and its effective application.

JOHN B. ATWATER, M.D., Dr. P.H.
Guest Editor

Planning for Coordinated Health Care

Franklin M. Foote, M.D., and George R. Walker, M.D.

During the past 20 years great changes in our society have had an impact on the entire health care system. Control of communicable disease and increasing longevity are changing the age distribution of the population. Although Connecticut's large cities are relatively stable in over-all population growth, they have absorbed many persons from low socioeconomic areas, while many of their former residents have moved out to the suburbs and beyond.

Public awareness of the meaning of new medical discoveries, of sophisticated and sometimes costly preventive, diagnostic and treatment advances has developed public expectation that the health professions should deliver to all of our citizens the best that modern medical science can offer. This expectation is particularly true in Connecticut, which prides itself on providing its people not only with a high level of material comfort but with many unusual cultural and intellectual opportunities.

New procedures that save lives and restore health like open heart surgery, the artificial kidney and high voltage or cobalt 60 radiation therapy are expensive, as are some of the newer and more complicated laboratory tests. At the same time there is a worsening shortage of personnel in the various health professions, similar to and perhaps even more acute than the manpower problem in education and social work. The ratio of physicians to other health personnel has changed markedly—in 1900 doctors of medicine constituted 62.7 per cent of professionally trained persons working in the health enterprise; by 1940 the ratio fell to 25.2 per cent and by 1960 to 21.3 per cent.¹ These changes present problems in continuing to organize health protective and health care services so as to provide the best possible quality protection and care within the limitation of resources available.

Demand for comprehensive broad spectrum health services are evident in the increasing role such fringe benefits play in labor contracts, and in the number of health statutes enacted by recent sessions of the U.S. Congress.

DR. FRANKLIN M. FOOTE, Commissioner and DR. GEORGE R. WALKER, health planning coordinator, Connecticut State Department of Health, 79 Elm Street, Hartford, Connecticut.

Federal Legislative Developments

Shortly after World War II Congress enacted the Hill-Burton program to help finance hospital, health center and rehabilitation center construction based on hospital service area planning regions, and vastly expanded medical research programs through the National Institutes of Health. In recent years came water and air pollution control measures and the Kerr-Mills program, to be followed by several far-reaching acts of the 89th Congress. Among the more important of these were Titles 18 and 19 of the Social Security Act, providing federal funds for home health care, out of hospital laboratory and medical services as well as care in hospitals and extended care facilities. Title 5 expanded crippled children and maternal and child health programs. The Heart, Cancer and Stroke Act provided for regional medical programs to set up cooperative arrangements between medical centers and other health facilities to control these and related diseases.

Programs of the federal Office of Economic Opportunity and of the new Department of Housing and Urban Development have among their goals improving the health of indigents, helping hospitals and other health facilities, pollution control, rebuilding deteriorated sections of cities. The latter agency requires clearance of certain health related projects with regional planning agencies within a state.

Hearings before the 89th Congress documented some of the shortcomings in the present intergovernmental arrangements for health. These included fragmentation in health programs, gaps in health service coverage, lack of rational planning, lack of coordination at state and local levels, undue rigidity in financing of categorical programs and inability to use scarce professional help efficiently.^{2a} A well-to-do uncomplicated hernia patient might have the entire attention of a registered nurse in attendance, while 8 or 10 other seriously ill patients might be served by a single nurse.

Worsening Shortage of Health Manpower

The state education department recently released findings of a study of the need for workers in the health enterprise conducted by the Labor Education Center of the University of Connecticut. It

found health services the most rapid growth field in the state, with 52,530 persons employed in June 1966, a 57 per cent gain over the previous ten years. Looking ahead it forecast a need for 59,214 additional trained persons in health services by 1976, including nurses but not including physicians, dentists and others requiring a college degree. The greatest need was pinpointed for registered nurses. Although the study disclosed that hospital and nursing home administrators preferred college graduates for nurse supervisors and instructors, three-year diploma school graduates were greatly preferred for staff nurses.³

Prior to World War II, any notion of social planning in America was viewed as subversive, possibly because of association with the concept of the Soviet Union's widely publicized five year plans and their close relation to the aims of international communism. Occasionally, however, a voice was raised about the value of studying trends in political thinking, of experimenting with a variety of ways to provide services to solve medical problems.⁴

During the second World War the need for comprehensive, economic as well as industrial planning became obvious in fighting a war in several parts of the globe. Such planning developed in the Atomic Energy Commission and has continued and broadened in peace time to permit best use of nuclear energy, to operate the department of defense more effectively, to develop space exploration and improve communication.

Within the past three years planning has arrived in health. Every state has developed mental health and mental retardation plans to meet fully needs in these areas for both construction and services, enlarging public recognition of problems previously dealt with only in small part under the Hill-Burton survey and planning activity. In 1966 an important planning effort began in Connecticut to develop machinery better to meet the needs of disabled persons under a \$200,000 Vocational Rehabilitation grant to the state department of education. Planning is also an important component of the Regional Medical Program for Heart, Cancer and Stroke that began in Connecticut in 1966.

In November 1966 the president signed Public Law 89-749 in which Congress declared that fulfillment of our national purpose depends on promoting and assuring the highest level of health attainable in an environment which contributes positively to healthful individual and family living, that "attainment of this goal depends on an effective partnership, involving close intergovernmental col-

laboration, official and voluntary efforts, and participation of individuals and organizations." The act provided for comprehensive planning for health services, health manpower and health facilities in order to assure high quality health care for every person without interference with existing patterns of medical and dental practice.⁵

State Health Planning Council

Public Law 89-749 provides for setting up a statewide health planning council in each state to include representatives of both governmental and non-governmental state and local agencies concerned with health, with the majority of the members of such a council consisting of consumers of health services. The Connecticut State Medical Society is among the professional associations represented on the council, and the consumers reflect geographic, socioeconomic and ethnic groups. The council held its first meeting on March 26, 1968 under the chairmanship of Mr. C. Manton Eddy of West Hartford.

The state planning council advises the state health department, the agency designated by Governor John Dempsey to administer or to supervise the administration of the activities to be carried out. These activities will include the setting of goals, collection of data to assess health needs and the existing resources that are available to meet physical, mental and environmental health needs of all the people of the state, and establishment of methods to determine priorities in highlighting critical problems requiring early attention.⁶

An integral part of the statewide comprehensive health planning effort will be the setting up of committees, task forces and other groups to study specific problems. Some such groups have been active for some time such as the Clean Water task force—others such as the Clean Air task force, Drug Dependency Advisory Council, Child Day Care Advisory Council and epilepsy study council were authorized by the 1967 General Assembly. In 1967 by executive order Governor Dempsey created a rodent and vermin control committee. Connecticut's office of health planning will have liaison and work closely with all such groups in whatever way is appropriate, serving to bring together meaningful judgments and opinions as well as factual information in such a form that it will be useful in working out various alternate solutions to the problems presented. Focus will be on long range planning, broad concepts and trying to reach a consensus as to basic philosophy.

The Advisory Council on Comprehensive Health Planning has designated six commissions which are initiating discussions within their respective fields of work. These are: Aims and priorities, health manpower, health care facilities, personal health services, environmental health, and regional and local planning and organization. An executive committee holds meetings between council meetings in order to maintain close touch with activities.

It is significant that the Congress recognized the proper role of states in studying health problems and establishing priorities in meeting identified needs. Despite the strong involvement of federal funds in health research and services, constitutional responsibility for protecting and promoting health is reserved to the states. The Supreme Court declared in 1911, “. . . Among the powers of the State not surrendered—which power therefore remains with the state—is the power to so regulate the relative rights and duties of all within its jurisdiction as to guard the public morals, the public safety, and the public health, as well as to promote the public convenience and the common good.”⁷

Federal action to provide for state and metropolitan area planning followed closely on publication of a four year study of community needs by the National Commission on Community Health Services, sponsored by the American Public Health Association and the National Health Council. Their leading recommendation was that, “Each state should have a State Health Policy and Planning Commission, responsible to the governor, which would advise him on health planning for the state.”⁸

Regional Planning Within Connecticut

Public Law 89-749 provides further for grants to aid in setting up agencies to conduct health planning for regions, metropolitan areas or other local areas. Purpose of such agencies is to contribute to the statewide planning effort by stimulating community discussion, identifying health goals and local needs, initiating action to coordinate for maximum use all existing and planned facilities, manpower and services in the areas served. Regional groups likewise will collect data, provide informational services to insure communication of planning progress and decisions to the public and to appropriate organizations in the area that have a role in health planning. Metropolitan planning groups may comment upon financial, organizational, jurisdictional or other impediments to effective

use of existing resources, or may suggest new uses for these resources.⁹

For these local or metropolitan area planning agencies there is to be a board or council similar to the statewide council representing major governmental and voluntary organizations concerned with public health, with the majority of the board representing consumers of health services. In Connecticut there already are several community councils serving metropolitan areas which might take the initiative in setting up health planning organizations. Since 1957 by direction of the General Assembly the state development commission has defined 15 planning regions, the majority of which are well organized with full-time planning directors. A health planning agency may be organized in close coordination with one or more of such regions, each of which has a governing body composed of town and city officials as well as business and civic leaders. In the beginning these regional agencies were concerned chiefly with planning for land use, transportation, open spaces and attracting suitable industry, but more recently they have turned to problems of human needs, sanitary facilities, social services.¹⁰

In July 1968 the Health Facilities Planning Council of Greater Hartford and the Greater New Haven Community Council each received federal developmental grants looking toward the formation of comprehensive health planning agencies in the Capitol and South Central planning areas respectively.

Complementary Relations with other Planning Groups

Fear has been expressed in some quarters that a statewide comprehensive-health planning effort may duplicate or conflict with planning efforts already under way in certain segments of the broad field of public health. The chairmen of the congressional committees concerned recognized this feeling. In presenting the bill Senator Lister Hill stated “The comprehensive planning of the state health planning agency with the advice of the council would complement and build on such specialized planning as that of the regional medical program and the Hill-Burton program, but would not replace them.”¹¹ Representative Harley Staggers in advocating passage of the bill in the House of Representatives stated “The new state health planning agencies would not supplant existing planning mechanisms in specialized programs. For example, hospital and other health facilities construc-

tion programs, mental retardation programs, or construction of community mental health services. Rather, the bill is designed to help bring order into the statewide planning process, which is now spotty and fragmented. It would provide, for the first time, resources to measure and understand the special health needs of each of the states, and would make it possible to establish priorities for meeting these needs."^{2b}

In order to clarify relationships between comprehensive health planning and the Heart, Cancer and Stroke Amendments of 1965, the Office of the Surgeon General has issued a statement outlining the scope of each program, processes and relationships. This statement explains that comprehensive health planning is to provide assistance in the development of more effective relationships among the several existing health programs and to provide a better basis for relating these programs to the accomplishments of over-all health objectives at the state and local level. The federal statute recognizes that accomplishment of improvement in the quality and coverage in health service, both personal and environmental, depends on the voluntary participation and energies of both private and public sectors of the economy. Finally the Public Health Service statement declared its intent "to prevent waste of scarce resources through useless duplication" and to develop ways of promoting effective coordination between all of the varied grant programs coming under its control.¹²

In making a study of a community problem in order to plan a well coordinated attack, some of the methods of epidemiologic investigation can well be used.¹³ The problem needs to be defined in terms that will be clearly understood by all concerned. Extent, nature, significance and severity of the problem may be explored. One then may assemble information about the natural history of the problem, how factors pertaining to the host or individual involved, the outside agents influencing the problem and the environmental patterns all may affect its extent. The next step, if such steps may be separated logically, is to ascertain at what points control measures may be effective, with emphasis when appropriate on earliest possible prevention.

After determining the various control measures that might be applied to reduce or eliminate a problem, one generally selects among these that which appears to be most promising in offering effective control. One makes an inventory of all possible resources that might be mobilized to control the problem, including status of scientific knowl-

edge, services already at least partially organized and manpower that is available. After these investigations have been reasonably complete, a planning group such as a regional or statewide health planning council is in a position to consider and decide which health problems are so serious as to require an immediate attack, and how the various resources available can be brought together to bring about an early and effective solution.

Despite this outline of the purpose and detailed machinery for planning, it is my hope that planning by councils, committees and task forces will not hinder individuals or other organizations from following their own sideroads, creating new and imaginative solutions to problems, presenting well thought out opposing points of view. There is a tendency in this computer age to assume that if a man's life, infirmities and clinical chemistry are encapsulated within the scope of a tape or a punch card, adding up the columns produces a mystique with which no human can argue. I hope we can avoid the limitations and pitfalls ably described by William H. Whyte, Jr. whenever a detailed master plan is evolved.¹⁴ While trying to give leadership and coherence, it is urgent that hunches, emotional attitudes and inspiration be recognized as contributing to the way the signals may be called at any particular moment.

When goals are described, solutions suggested and priorities recommended, in the field of health these are not and cannot become a static blueprint to be followed blindly. Planning will be a continuous process. Questions should be raised, evaluation methods undertaken appropriate to various operating programs, and the tentative plan modified or even cast aside if indicated. In fact the greatest benefit of the planning effort may be the start of a productive and continuing dialogue between the consumers of health care and the professionals. Out of such give and take may come not merely greater wisdom but improved understanding by all who will be involved.

References

1. U.S. Department of Health, Education and Welfare Public Health Service Division of Public Health Methods, Chart Book on Health Status and Health Manpower, page 30, 1961.
- 2a. Stagers, Harley, Chairman Committee on Interstate and Foreign Commerce, Report 2271 to accompany H.R. 18231, Comprehensive Health Planning and Public Health Service Amendments of 1966, page 3, October 13, 1966.
- 2b. *Ibid*, page 5.
3. Labor Education Center, University of Connecticut: Health Service Occupations, Connecticut State Department of Education, Hartford, 117 pages, September 1967.

4. Root, Maurice T.: An Everyday Approach to Some Pressing Medical Problems, Hartford Hospital Bulletin, Vol. 1, pages 5-9, May 1938.
5. Public Law 89-749 Comprehensive Health Planning and Public Health Services Act of 1966, U.S. Congress, 11 pages, November 3, 1966.
6. Regulations Governing Grants to States for Comprehensive Health Planning, Title 42 Public Health, Chapter 1, Subchapter D, Part 51, Federal Register, Vol. 32, pages 10792 to 10794, July 22, 1967.
7. House vs Mayes, 219 U.S., page 270 at 282, Justice Harlan, January 9, 1911.
8. National Commission on Community Health Service, Health is a Community Affair, page 197, Harvard University Press, Cambridge, Massachusetts, 1966.
9. Office of the Surgeon General, Information and Policies on Grants for Comprehensive Areawide Health Planning, Public Health Service, Department of Health, Education and Welfare, Washington, D.C., 21 pages, August 30, 1967.
10. Connecticut Development Commission, Steps to Establishment of Regional Planning Agencies in Connecticut, 23 pages, State Office Building, Hartford, 1966.
11. Hill, Senator Lister, Comprehensive Health Planning and Public Health Service Amendments of 1966, Report of Committee on Labor and Public Welfare, Calendar No. 1632, page 5, September 29, 1966.
12. Office of the Surgeon General, Fact Sheet: Complementary Relationships between Comprehensive Health Planning and Public Health Services Amendments of 1966 and the Heart Disease, Cancer and Stroke Amendments of 1965, U.S. Department of Health, Education and Welfare, 9 pages mimeo., 1967.
13. Leavell, H. R. and Clark, E. G., Preventive Medicine for the Doctor in his Community, McGraw Hill Book Co., New York, page 623, 1958.
14. Whyte, William H. Jr., The Organization Man, pages 244-253, Simon and Schuster, New York, 1956.

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The Diagnosis Of Industrial Intoxications

Robert E. Brubaker, M.D.

Most physicians are familiar with the potential hazards of chemical products in the home either through the experience of practice or their own family living. In household intoxications, the effect of the harmful agent is actually or potentially immediate, the cause and effect relationship is usually clear-cut, and the sources of information and consultation, especially the Poison Information and Poison Control Centers, are well known.

In contrast, a significant number of toxic reactions in industry are low-grade and less obvious in onset, may be characterized by long-delayed effects, and may be difficult to relate to an exposure. Furthermore they frequently require special diagnostic considerations and sources of information and consultation which may be unfamiliar. The effect in this type of intoxication may be exactly similar to disease states not related to occupational exposure and the differential diagnosis may be difficult and time consuming. In almost all cases of this kind, a critical evaluation of the chemical agent in question and a review of the work environment is required.

In view of the ever increasing use and development of chemicals in industry, more physicians will have occasion to make diagnostic evaluations of patients suspected of intoxications arising from agents in the environment to which they are exposed at work. It is the purpose of this paper to review some important components of this evaluation and to point out some useful sources of consultation.

Investigation of the Chemical Agent

In industrial intoxications, the route of entry of the agent into the body is usually by inhalation, sometimes by skin absorption, but infrequently by ingestion. Whatever the route, a thorough evaluation of the suspected substance must be made. Indeed, a decision for or against an intoxication may turn on this. The following questions must be answered in making the evaluation:

1. What is the exact nature of the agent? It is not enough to know only the general nature of the agent because, for example, the salts of metals may be more or less toxic than the

metal itself, or in the case of organic substances substitute groups may render the original chemical much more toxic or conversely harmless. Furthermore, many chemicals of somewhat similar names have diverse effects. Unless one is sure of the specific structure of the chemical in question, uninformative and misleading studies may be done.

2. How likely is the agent to have entered the body? The fact that a chemical may be potentially toxic does not necessarily indicate that it will be harmful to human beings. It must first enter the body. Whether it does so will depend on its physical state and the manner in which it is used. As an illustration, certain metals are perfectly harmless when handled in the solid state but extremely hazardous when volatilized in a fume by the heat of machining or welding. Again, some substances may present a hazard only when used in a liquid form which may be absorbed through the skin.

With regard to usage, even though a chemical may be toxic, the process in which it is used may be so well designed or the protective equipment so adequate that contact with the worker is not possible. Of course, the adequacy of protective devices must be determined by investigation.

3. What quantity did the patient receive? This is the most critical question of all. The fact that a worker was exposed to a potentially harmful substance in his working atmosphere is not in itself evidence that he has been damaged by it. The question is: *To how much* of the substance was he exposed? The concept of dosage (i.e. the concentration of a substance multiplied by the time a worker was exposed) is basic for the correct appraisal of industrial intoxications. Some chemicals have such high toxicity that they must be used in closed systems. For the vast majority of substances, it is not practicable, nor is it necessary, to render the work environment completely free of the substance. It is necessary, however, to limit exposure so that no harm will result to the worker. How can this limitation be assured?

From the Medical Department of the Olin Mathieson Chemical Corporation, New Haven.

Each year the American Conference of Governmental Industrial Hygienists publishes a list of several hundred chemical substances with Threshold Limit Values for each one. A figure is assigned to each substance which represents the average concentration (expressed in parts of the substance per million parts of air in the case of gases and vapors, or in milligrams of the substance per cubic meter of air in the case of metals) to which a worker may be exposed safely for eight hours per day five days per week. Since these values are based on an exhaustive review of current toxicologic research and of industrial experience, they influence safety standards for all industry. Industrial equipment and procedures are designed to keep exposures to potentially harmful substances within these recommended limits in areas where workers can breathe them, and routine air measurements are made for substances in use to assure that where potential exposures exist these Threshold Limit Values are not exceeded. While the American Conference of Governmental Industrial Hygienists is a private organization, its recommendations have been incorporated into the regulations pertaining to Federal public contracts covered by the Walsh-Healy Act, and into the Public Health Code of the State of Connecticut thereby legally obligating industrial organizations to abide by them.

Whenever a suspected toxic exposure is under consideration, the quantity of the agent the patient received must be considered in relationship to these values. Air concentrations below the Threshold Limit Values would be evidence against a toxic exposure although instances of hypersusceptibility do occur.

4. Is the toxic substance in question known to produce the signs and symptoms the patient presents? The effects of the vast majority of chemicals used in manufacturing operations are wellknown on the basis of acute and chronic toxicologic studies in animals and of cumulative industrial experience among exposed workers. The absence of an appropriate clinical picture will, therefore, provide enough evidence to rule out the suspected agent as the cause of the illness in question.

In chemical research operations, in contrast, the effect that a new chemical might produce is often not known, and as a consequence,

cause and effect relationship may be difficult to establish. The purpose of research is to develop new compounds and although the degree of toxicity of these may be inferred from their structure, one does not have initial knowledge of the previously discussed characteristics of the agent which are necessary to reach an informed opinion in the case of a suspected intoxication. Such compounds must be handled as if they were harmful until toxicologic information can be developed.

To summarize the investigation of the agent in making a differential diagnosis of a suspected chemical intoxication, one must know the exact nature of the agent, the probability of its having entered the body, and the amount of the substance to which the patient was exposed in quantitative terms. Finally one must always relate this agent evaluation to the clinical findings in the patient, against the background of existing toxicologic data.

Evaluation of the Environment

A survey of the work environment should always be done in considering the possibility of an industrial intoxication. Good room ventilation and adequate air exhaust at the work-site, thorough training of employees in the handling of toxic materials, and good supervision are all evidence of attention to safety and interest in the protection of the health of employees. Lack of attention to these details when correlated with other findings would lead one to suspect the possibility of the dissemination of a harmful agent. The environment should also be examined for other agents which may themselves account for the clinical findings or which may act as synergists.

One must also inquire into the patient's home environment, his recreational activities, and into the possibility of a second job.

The Clinical Work-up of the Patient

The clinical examination may proceed from one of two viewpoints. In the first, the patient raises the question of a work-related disease as his presenting complaint and the clinical investigation follows. In the second, the clinical examination has already been made, for example in liver, hematologic, or neurologic disease, and the physician wishes to consider the possibility of an industrial exposure to explain the findings. In either case, the same evaluation of the agent and environment and the correlation of the findings with the signs and symptoms must be made.

The History

All symptoms, past and present, must be recorded especially in sequential relationship to possible toxic exposures at work, at home, in recreational activities, and at a second job. In some cases a patient may report that in the early weeks of his illness he had symptoms during the work-week with relative recovery over the weekends. Later on, symptoms may have been present more constantly. Such a history might well indicate an exposure to a toxic substance at work.

One important point with regard to a history of a possible toxic exposure at work must be emphasized: the history as reported initially by the patient can rarely be considered as clinical evidence either for or against intoxication. This is not due to attempts to conceal or distort on the part of patients, but simply to the fact that many patients cannot differentiate significant from insignificant points. All items in the history should be checked for accuracy and relevancy by evaluating the agent and the environment at the work-site.

The Physical Examination

Some chemical agents give rise to signs and symptoms which are highly suggestive of their effect, but many others produce clinical findings in various organ systems which are indistinguishable from those resulting from other disease agents. The absence of positive physical findings does not in itself rule out an industrial intoxication since some agents produce symptoms rather than signs. An accurate diagnosis can only be made after correlating the physical examination with the history, pertinent laboratory analyses, and the detailed information regarding agent and environment.

Laboratory Studies

Some substances or their metabolites can be measured in body fluids. There are now a number of enzyme determinations of diagnostic significance, and tests of even greater sophistication are currently being validated. Examination of the patient's expired air can sometimes be helpful. For example, if samples of the expired air can be measured in sequence for the concentration of a given solvent, one can construct an excretion curve which can be extrapolated back to the original air concentration the patient breathed at the time of exposure. Specific suggestions for laboratory analysis can be outlined by consultants as suggested later. These specialized tests must be done in laboratories with experience in the techniques required.

The Emotional Aspects of Industrial Intoxications

Any discussion of industrial intoxications, however brief, must include some mention of emotional factors, for they can make the diagnosis and the diagnostic process more difficult. Among workers who are aware of a potential toxic hazard, there will often be some anxiety. Sources of frustration and discontent both in-plant and out-of-plant may augment this anxiety. Feelings of anger due to friction with fellow-workers or with the supervisor, emotional stresses at home, or the effects of indeterminate internal stresses may be displaced onto the problem of real or alleged intoxication, which may thus become the focus of quite unrelated difficulties.

Even when an agent in question is known to produce certain specific somatic changes, it may not be easy to sort out emotional components. When one must consider further a possible intoxication from an agent which is known to give rise to vague neurologic signs and symptoms the diagnosis may be most difficult. The symptoms of neurosis and of early systemic disease may be quite similar: fatigue, headache, dizziness, feeling of pins and needles in the extremities, gastrointestinal and cardiovascular symptoms, irritability, and lack of concentration.

Symptoms will sometimes occur in a group of people working together, and it will then be necessary to interview a number of them at least, and the supervisor as well in order to gain some understanding of the exposure or of the possible contagion of the idea of exposure from person to person.

Patients are usually quite sincere regarding their complaint that they have been injured by a chemical exposure at work, and often they are so convinced that they come to the physician for confirmation only. If they are emotionally upset, particularly by feelings of anger and frustration at work, they may interpret a careful appraisal of all the related factors and a detailed examination as an expression of disbelief on the part of the physician or an attempt to negate what they already believe is a fact. Thus the physician-patient relationship may be strained.

During the time a differential diagnosis is under consideration, it is most important that the physician should not indicate in any way that an industrial intoxication is present, especially in patients who are emotionally upset, unless this has been determined beyond doubt. A premature implication or remark may greatly reinforce the patient's

own belief that his illness is due to a work-related exposure. If an intoxication is confirmed, no additional emotional complication will result. But if it is finally determined that the illness is not work-related and due rather to another disease, the patient may then be entirely unable to accept the alternate diagnosis even though the evidence for it may be conclusive. In such a case, Workman's Compensation adjudication will undoubtedly arise and, unfortunately, the attention of all concerned may center on the controversy rather than on rehabilitation and return to work.

Sources of Information and Consultation

Most physicians, including those working full-time in occupational medicine, will usually need to rely on consultants for the evaluation of agent and environmental aspects of a suspected industrial intoxication and for assistance in selecting and interpreting appropriate laboratory work. What kind of consultants does one need and where can they be found?

The consultants are from two highly specialized fields: Industrial Toxicology and Environmental Hygiene Science. The industrial toxicologist knows the physiological effects of chemicals. He may be able to supply information on the probability that the specific signs and symptoms in a patient could be caused by a specific chemical. He will also be able to suggest specific clinical laboratory tests most likely to yield valid diagnostic data.

The environmental hygiene scientist (industrial hygienist) can answer such questions as: Is the information given by the patient regarding a toxic exposure correct? What is the probability the agent entered the body through inhalation, skin absorption, or by ingestion through transfer from hands to cigarettes or food? What is the range of concentration of the chemical in the atmosphere of the patient's work environment? What is the relationship of these findings to the allowable Threshold Limit Values for occupational exposure?

Where can such information and consultation be obtained? The physician should first contact the manufacturer or company involved as soon as he suspects a work-related intoxication, and he should expect prompt cooperation and assistance. Many large companies have industrial toxicologists and industrial hygienists on a fulltime basis. Smaller companies may have such consultant available on a private arrangement or through an insurance carrier.

If sufficient information is not available through the company, or if the physician wishes an inde-

pendent consultation an excellent resource is the Section of Occupational Health of the Connecticut State Department of Health. This section is headed by a specialist in occupational medicine and toxicology, and is staffed by an occupational health nurse consultant, industrial hygienists, industrial ventilation engineers, and radiation health physicists and technicians. A large library is available together with personnel to look up any information a physician may request. Its services include telephone consultation on aspects of differential diagnosis, and surveys of the work environment by industrial hygienists the results of which the physician may utilize in reaching a diagnostic conclusion. Specialized analytical procedures can be performed by the Laboratory Division of the State Department of Health. Inquiries should be directed to Dr. Joseph Stapor, Section of Occupational Health, Connecticut State Department of Health, 79 Elm St., Hartford.

Finally, it should be remembered that physicians are legally required to notify the State Department of Health of a diagnosis of an occupational disease.

Summary

1. When industrial intoxications are acute, cause and effect are relatively easy to establish.
2. Subacute and chronic intoxications, especially those in which the effect is gradual or delayed, are often indistinguishable from other diseases on clinical examination, and the cause and effect relationship may be very difficult to determine. In these cases it is necessary to make a thorough appraisal of the agent and of the environment, and to do specialized laboratory procedures when appropriate in order to decide for or against causal relationship. Consultation with industrial toxicologists and industrial hygienists may be necessary.
3. Sources of information and consultation are:
 - a. The company, which should be contacted promptly when an intoxication is suspected.
 - b. The Section of Occupational Health of the Connecticut State Department of Health.

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Connecticut Regional Medical Program — From Planning To Operations

Edward F. Morrissey, M.S.W., Conrad A. Seipp, Ph.D. and Henry T. Clark, Jr., M.D.

C.R.M.P. Planning Activities to Date

On October 6, 1965, President Johnson signed P.L. 89-239, providing for education, research, training, and demonstrations in the fields of heart disease, cancer, stroke, and related diseases. In early November, 1965, Governor Dempsey appointed a committee of representative lay and professional health leaders of Connecticut, with Commissioner of Health Franklin Foote as Chairman, to recommend appropriate steps to implement the new law in this State. That committee included the President and President-Elect of the Connecticut State Medical Society as members and its General Manager as an adviser.

The resulting plan of action called for the Deans of the Yale and University of Connecticut Schools of Medicine, acting jointly, to develop a request for a planning grant for submission to the National Institutes of Health. The various health interests of Connecticut were to be involved, as appropriate, in the planning process and in the ultimate implementation of plans.

The two Deans activated an Advisory Board of 20 members, which was broadly representative of the public interest, with Mr. Arthur Rogers, an industrialist of Waterbury, as Chairman. An application for a planning grant was prepared by a special committee of university faculty members. This application was approved by the Advisory Board and sent to the National Institutes of Health in April, 1966.

In June, 1966, the National Advisory Council for P.L. 89-239 approved the Connecticut application as submitted. This was one of the first five such applications approved from across the United States.

During the July–September, 1966 period, four Conferences were established to aid the Advisory Board in its work. These four conferences con-

sisted of: (a) the presidents of the Boards of Trustees of the hospitals of Connecticut; (b) the chiefs of staff of these hospitals; (c) the administrators of these hospitals; and (d) representatives of over 50 "health" agencies of Connecticut. The first three of these held organizational meetings during this period.

The Director of the C.R.M.P. took office on October 1, 1966. His first deputy arrived on November 1.

During the October-December, 1966 period, the planning staff began to get acquainted with the health scene in Connecticut. In addition, they worked with a Planning Committee of university faculty representatives augmented by Commissioner Foote, Mr. Rogers, Dr. Orvan Hess, then President of the Connecticut State Medical Society, and Dr. Stewart Hamilton, then President of the Connecticut Hospital Association, to develop a specific plan of action.

That "plan for planning" was formalized in early January 1967, and officially adopted on January 12 by the Advisory Board as the Planning Design of the C.R.M.P. It was discussed in detail at four meetings of the Advisory Conferences which were held during February and early March, 1967.

As one of its provisions, the Planning Design called for the creation of nine task forces to study specific components of the Connecticut health care system, to determine deficiencies, to chart action programs and ultimately to work for their implementation. Each task force was to include representatives of various points of view appropriate to the topic under discussion, drawn from private practice, education, voluntary agencies, government service and the public-at-large.

During April and early May, 1967, the nine task forces were activated and began their functioning. These task forces dealt with the supply and distribution of physicians and dentists, the allied health professions, continuing education for physicians and dentists, extended care facilities and programs, university-hospital relations, organization of special services in hospitals, a state-wide medical library system, the financing of health care, and research and evaluation.

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DR. HENRY T. CLARK, JR., Director, Connecticut Regional Medical Program.

On June 1, 1967, an initial assembly of documents describing the current health scene in Connecticut was completed. These were augmented by a number of special studies for the C.R.M.P. staff. This information contributed in various ways to the deliberations of the task forces.

At its October 19, 1967 meeting, the Advisory Board reviewed the progress that was being made by the various task forces in their planning activities. The Board noted that the implementation of some of the developing plans would soon call for operating funds. The Board urged that steps be taken to carry the initial phases of planning to a conclusion so that an operating grant request could be submitted to the National Institutes of Health early in 1968.

The period from November, 1967 through February, 1968 witnessed intensive activity as the C.R.M.P. staff and task forces sought to comply with the request of the Advisory Board. The planning Committee reached a consensus on the elements of an operating grant request early in February and endorsed detailed operating budgets during an all-day meeting in mid-February. The Advisory Board gave unanimous approval to both program elements and budgets on February 21, 1968. Early in March an operating grant request was, accordingly, submitted to the Division of Regional Medical Programs in Washington. This application constituted an initial assemblage of program activities for which some \$24 million in support was sought for a five-year period.

C.R.M.P. Guiding Philosophy

The Connecticut Regional Medical Program, by terms of its legislative mandate, is dedicated to the provision of optimum patient care in the fields of heart disease, cancer and stroke and related diseases. All of the elements of the health care system in Connecticut—the two university medical centers and the other educational and research institutions within the state, the various state agencies and voluntary organizations involved in the health field, and the related practitioners—collectively share in this concern. The care of patients is the common end product to which each contributes. This common denominator of concern has been the base on which the C.R.M.P. has brought the various elements of the health system of the region together for planning purposes.

The nine task forces have emphasized, again and again, the need to strengthen cooperative arrangements of the medical care system in Connecticut.

The reason is to insure the delivery of comprehensive, high quality medical care to the entire population of Connecticut. Comprehensive care has many dimensions. It involves first of all completeness. It seeks to integrate prevention with treatment and rehabilitation, and to foster the active promotion of health and education for it. It seeks to maximize the availability and accessibility of quality care, provided on a multiprofessional basis and in a personalized manner. It also underscores the importance of continuity, both in the provision of care and in the assumption of responsibility for it.

Through the activities of the task forces it has become clear that regional coordination is a necessary organizational mechanism for the realization of this ideal. Regionalization is seen as the means for increasing the resources available to practitioners at the community level to provide the best possible care for individual patients.

Although the basic concepts of regional medical planning are several decades old, there are significant new elements in the current Connecticut health scene. There is, first, the commitment and active involvement of the two university medical centers in this enterprise. There are, furthermore, several other important health planning endeavors underway in Connecticut at this time which are related to this program and which should reinforce it. In addition, there exists in Connecticut an apparent willingness in many quarters to examine the medical care system critically and to chart new courses.

In order to appreciate all this more fully, we should examine the distinctive features of Connecticut as a medical care region. Connecticut, with a population approaching three million, is experiencing more rapid growth than any other northeastern state. Heavily industrialized, it ranks first among the 50 states in average per capita income. Although Connecticut is small in area, it possesses a number of medium-sized urban centers which are tied together by excellent highway systems. There are, nevertheless, substantial differences between its "urban corridor" and its more rural and peripheral sections. The region is served by a highly developed network of 35 voluntary, acute general hospitals and 15 public, specialized institutions. These are supplemented by more than 250 extended care facilities. There are in Connecticut 175 physicians per 100,000—one third more than for the country as a whole. The state has a corresponding advantage in terms of dentists, nurses and other categories

of health personnel. The many voluntary health agencies and organizations that function in Connecticut reflect a long tradition of public spirited concern and involvement in various facets of the region's health care system.

With the presence of the Yale University Medical Center, Connecticut contains within its borders one of the oldest and most esteemed institutions of medical education in the country. About one-tenth of the practicing physicians in the region are graduates of this school. There is emerging within the Medical Center, as within the University as a whole, a new sense of commitment toward community affairs. At the same time, with the development of the University of Connecticut Health Center in Farmington, which admitted its first medical and dental students in the fall of 1968, an important new resource for research, education and patient care is being introduced into the region. The University of Connecticut now possesses a wide array of schools of the health and health-related professions.

In a region which is so richly endowed with health resources, the problems of improving patient care do not center primarily upon the creation of additional facilities, the introduction of new technologies, or the augmentation of the supply of health manpower. Rather, the essential task is to meet the needs of the population at the local level in ways which more fully utilize the great resources already available.

The mission visualized for the Connecticut Regional Medical Program is to identify, promote, and assist in the organization of the optimum relationships and functional linkages among the various elements of the health care system of Connecticut. Given its emphasis upon strengthening local performance, the program faces in two directions. *On the one hand*, the program seeks to stimulate organized and sustained planning within the various health service areas of the state. The aim of such planning should be to foster the development of the fullest working arrangements among community hospitals, the various extended care facilities and programs, the public and voluntary health agencies and the community-based practitioners. *On the other hand*, the C.R.M.P. seeks to ascertain the ways in which the two university medical centers and the other major resources of the Connecticut region can best make available their specialized competencies and skills as technical backstopping and reinforcement to the practitioners and institutions which render care at the local level.

Connecticut is an essentially self-contained medical care region. The various elements involved in the provision of medical care are so located that it is possible to identify a number of major focal points which serve to define more or less sharply the existing patterns of patient movement and professional practice. As a working basis for the program, the state has been divided into ten health service areas. The accompanying map indicates this division.

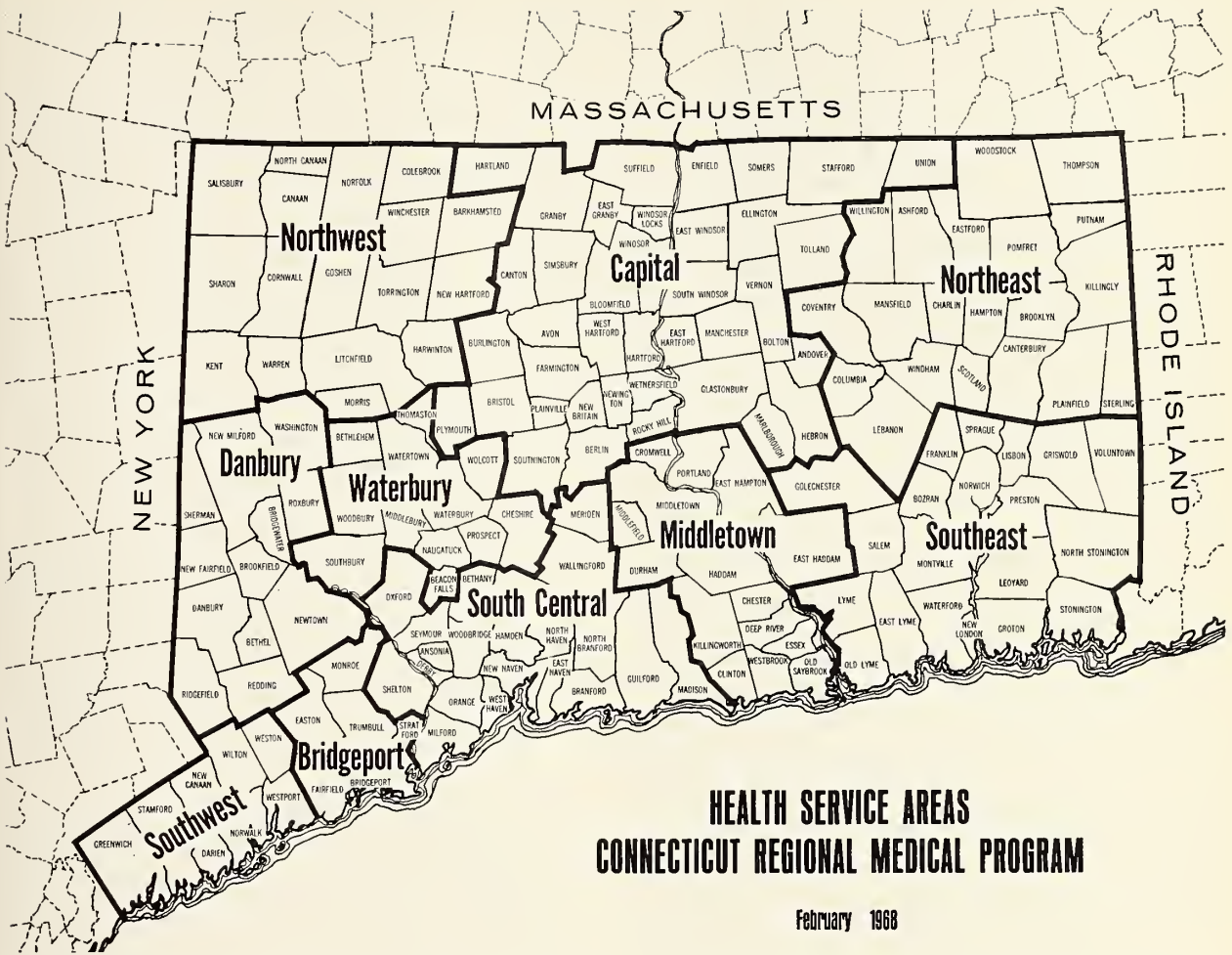
Attention has been given to the correlation of these health service areas with the regional planning activities of other Connecticut health agencies. It is noteworthy that the State Hill-Burton Agency, the Connecticut Hospital Planning Commission and two local health planning agencies within Connecticut adopted this map months ago and that the State Department of Mental Health is reconsidering those instances where its delineation of the state departs from this division. This map was also adopted in the fall of 1968 by those responsible for planning patient care programs under P.L. 89-749.

Each of these health service areas commands a sufficient range of resources to function as a relatively self-sufficient and discrete component of the Connecticut medical care region. However, there are important differences among them. The largest area which centers upon the state capitol has ten times the population of the smallest in the north-western part of the state. There is an even greater disparity in the medical care resources which these ten areas command. Each, nonetheless, possesses at least two hospitals and is viewed as having the capability of service as a primary level of a regionalized system for the provision of comprehensive, quality health care.

Summary Of Thrusts Proposed For Beginning C.R.M.P. Operating Program

In this context the *first thrust* of the operational activities of the Connecticut Regional Medical Program is to promote efficiency and continuity of patient care in each of the ten health service areas of Connecticut. This has been a recurrent theme in the deliberations of the several task forces in recent months. As a consequence, funds were requested in the Operating Grant for the following:

- A. To assist in the development of a program for the routine assembly of patient care information. At the outset this information will be assembled on all hospitalized patients, but the collection will be extended in time to



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out-patients and to patients in long term care facilities. The information obtained will be made available in various ways to individual practitioners, to utilization review committees, to administrators and planners, and to researchers. It will be useful in promoting better patient care in individual cases and in providing guidance for the development of an optimum overall medical care program. Proper consideration of matters of confidentiality of information and patient consent must be built into the system.

- B. To stimulate and assist in the development of sub-regional health care planning in each of the ten health service areas of Connecticut for the most effective programming in the fields of heart disease, cancer, stroke and related diseases. It is felt that any local health planning activities launched for this purpose will contribute greatly to the planning of overall programs for personal health services.
- C. To assist in the development of at least one major demonstration of cooperative program-

ming between general hospitals, selected nursing homes, home health services and rehabilitation centers, looking toward the development of optimum medical care for victims of heart disease, cancer, stroke, and related diseases. This demonstration will be designed to stimulate comparable developments in other parts of Connecticut and beyond. It is evident that the development of the linkages proposed here would benefit many types of patients and not merely those with heart disease, cancer and stroke.

- D. To cover the costs of operating a series of patient care workshops which will be held in a wide variety of locations throughout Connecticut. These workshops will explore the need in local communities for continuity of patient care and demonstrate ways in which this need can best be met locally.

The above proposals concern approaches to improving the effectiveness and efficiency of patient care at the local level. However, the local health service areas are not technically autonomous or

professionally self-contained. They draw upon and make use of the more specialized resources for the care of patients which exist at the state level.

The *second major thrust* of the proposed C.R.M.P. operating program therefore, is to assist in creating more workable bridges between the health service areas and the centers of medical care which serve as resources for the entire region. This calls, first of all, for the development of working partnerships between key hospitals and one or the other of the university medical centers. The creation of a "third faculty" of the schools of medicine through the joint appointment of full time chiefs of service in selected hospitals throughout the region is visualized as the primary vehicle for this purpose. These physicians and dentists, together with necessary supporting staff, will be based in a local hospital but will be expected to spend a part of their time in the university medical center. In turn, the clinical faculty at the university center will be augmented to provide counterparts to the full time hospital appointees.

In the C.R.M.P. view, the community hospital-based "third faculty" will assume multiple roles. First, it will create an environment in a number of community hospitals in Connecticut in which some medical and dental student instruction will be given in the future. Second, it will contribute substantially to the quality and scope of intern and residency training programs in many Connecticut hospitals. Third, it will serve as a major force for the organization and provision of continuing education activities for practicing physicians, dentists and other health professionals. Fourth, it will be available, through consultation, to assist in the management of selected patients. Fifth, it will participate in the analysis and evaluation of patient care in the hospital it serves and throughout the surrounding health service area. Sixth, it will provide leadership for the development of many specialized medical services in the hospital it serves and thereby, in time, produce a greater level of medical self-sufficiency at the local level. Seventh, it will expedite and facilitate the process of selected patient referral to the university medical centers. And eighth, it can be expected to contribute to the planning and coordination of all medical care activities in its health service area, including medical care programs for the disadvantaged segment of the population. In all of these respects this "third faculty" will help mobilize outside medical resources, as appropriate, and will act as conduits for bringing the expertise and special capabilities

of the universities and the other regional resources into medical practice at the local scene.

The *third major thrust* of the proposed operating grant concerns the most effective ways of rendering certain specialized and technical services to the patients and to the physicians of Connecticut. This responds to the fact that rapid scientific advances in recent years have led to many new developments in diagnosis and therapy which call for scarce and highly skilled personnel and/or costly facilities and equipment. Study has been given to the development of selected services on a centralized basis in Connecticut and, alternately, to the strengthening of other specialized services on a decentralized basis. This has pointed to the urgency of including the following in the request for an operating grant.

- A. Funds to develop more effective programs in all acute, general hospitals of Connecticut for victims of coronary heart disease.
- B. Funds to develop a coordinated program of high energy radiation for victims of cancer in selected hospitals of Connecticut (During November, 1968, this proposal was withdrawn for further study.)
- C. Money to support the planning and first stages of development of a regional reference laboratory to augment existing laboratory capabilities within the region.

The *fourth major thrust* of the proposed operating program concerns the fuller development of selected programs of education for the health professions. Current activities in Connecticut in the field of continuing education for physicians and dentists have been found to be a hodge-podge, uncorrelated, with multiple sponsorship, reaching a limited audience and having doubtful effectiveness.

There is no overall plan or a clear delineation of objective in regard to a total program for the recruitment, training, distribution and continuing education of nurses and allied professionals in Connecticut.

Requests have therefore been made for the following:

- A. Funds to coordinate and expand programs for the continuing education of physicians and dentists through: (1) the establishment of a central coordinating agency; (2) the creation of special information centers at each of the two university medical centers; (3) the utilization of the potentials of the educational television network which is currently developing under State auspices; and (4) the establish-

ment of a number of refresher fellowships to enable selected practitioners to return to the university setting.

- B. Funds with special regard to nurses and allied health professionals; (1) to develop and maintain an inventory of health profession education programs and facilities; (2) to support a series of expert advisory committees concerned with such matters as counseling and recruitment, curriculum design, coordination of basic-clinical aspects of education, and licensing and accrediting; (3) to expand and decentralize continuing education programs; (4) to assist existing organizations in the development and implementation of counseling and recruitment programs for the health professions; and (5) to develop in time a health profession education council.
- C. Funds to strengthen the medical and allied library resources and services throughout Connecticut by expanding the capacities of the two University Health Libraries to render services to practitioners and institutions in the region and by developing the library program at the periphery.

The *fifth major thrust* of the proposed operating grant request concerns the continuing assembly and analysis of data on the medical care programs of Connecticut in order to provide a sound guide to the development of C.R.M.P. operating activities and to evaluate the results of these activities.

In its simplest form, this calls for bringing together statistical information about ongoing health activities in Connecticut, which is largely being collected now on a routine basis by the State Health Department, the Connecticut Hospital Association, Connecticut Blue Cross and a number of other agencies. In its more complex form, this activity calls for the most sophisticated research in the organization and delivery of health care.

The proposed C.R.M.P. operating grant request calls for support for the following:

- A. Funds to maintain a continuing inventory of health resources and services available in Connecticut, organized to reflect developments in regionalization.
- B. Funds to support a study of physician office practice in Connecticut and, in time, a similar study of dental practice.
- C. Funds to support a study of the patterns of care provided to selected patients with heart disease, cancer and stroke, and the impact,

over time, on mortality, morbidity and disability.

- D. Funds to develop the pilot phases of other important studies, such as emergency and out-patient services in Connecticut hospitals and intern and residency training in those hospitals.

The *sixth thrust* of the proposed operating grant request concerns the financing of health care. A great deal more information is needed about the costs of operating the present system of medical care in order to chart the most effective program for the future. Within this broad spectrum, more information is needed about financial implications of specific aspects of regional medical planning and programming in order to help chart definitive courses of action.

The C.R.M.P. operating grant therefore called for funds to provide assistance in undertaking selective studies in the field of financing hospital care, to be carried out in collaboration with the Connecticut Hospital Association, the Connecticut Blue Cross, Commercial Insurance Companies, the Connecticut State Medical Society and various branches of State Government.

The *seventh thrust* of the proposed operating grant provides for core staff to implement and evaluate the various aspects of the operating program and to continue planning for the optimum regional medical program for Connecticut.

Recent C.R.M.P. Program Developments

During the spring and summer of 1968 the focus was on expanding the base of understanding and support for the Connecticut Regional Medical Program through many meetings with individuals and organizations and on putting in motion numerous tooling up or pre-operational activities to prepare the way for implementation once the operating grant is approved. The C.R.M.P. staff was also involved in preparing for and participating in an extensive review of the grant application by the Division of Regional Medical Programs in Washington.

In this last connection, a site visit was made to Connecticut in mid-June, 1968, by a team representing the National Advisory Council of Regional Medical Programs. Subsequently, Washington officials stated informally that the visiting team gave a strong endorsement to the CRMP grant request. However, when the National Advisory Council met in Washington on August 26 to take action on the Connecticut request, it encountered a major cri-

tique from the Council of the Connecticut State Medical Society taking issue with some aspects of this request. As a consequence, on August 26, the National Advisory Council voted to defer action on the CRMP proposal to allow time for full discussion of different points of view of the CSMS and the CRMP.

In early September both organizations designated official liaison committees, and five meetings were held, the last on October 25. Of the 18 elements in the Operating Grant Request, the conferees reached agreement on 17. They further agreed that the 18th (the Regional Radiation Therapy Plan) should be given further study. The results of the conferences were reported back to the parent bodies of the two committees and the joint statement was made an official supplement to the CRMP Grant Request. Another site visit by a team from the National Advisory Council was then made to Connecticut on November 18, 1968, at which time CSMS spokesmen had a full opportunity to be heard.

On November 25, the National Advisory Council for Regional Medical Programs met in regular session in Washington and authorized three years of operating grant support to the Connecticut Regional Medical Program. The level of authorization for direct expenses for 1969 was \$1,634,000 (54% of request); for 1970, \$2,372,000 (61% of request); and for 1971, \$2,510,000 (62% of request).

During December, 1968 and early January, 1969 the CRMP staff, Executive Committee and Advisory Board were active in reviewing the proposed program elements in order to establish priorities and revise budgets to conform to the financial restrictions of the prospective grant award for 1969. It is anticipated that this process will be completed and the first year operating activities will be underway by February 1, 1969.

One other point deserves mention. As the first stage of CRMP planning activities neared completion in the spring of 1968 and the scope of the proposed operating program became evident, the two deans recommended that the stewardship of the CRMP be transferred to a body more officially representative of the public interests of Connecticut. As a consequence, a revised Organizational and Operating Structure for CRMP was adopted by the outgoing Advisory Board on June 6, 1968 (amended on September 12). The new Advisory Board will function, in effect, as a Board of Di-

rectors or Trustees of the C.R.M.P. It is made up of 36 members, covering the whole gamut of health interests in the state. This includes seven spokesmen for the general public. This new Board held its organizational meeting on October 9, 1968, and has been meeting in regular session since that time.

Conclusion

In summary, the Connecticut Regional Medical Program has pursued a broad spectrum of planning studies through the mechanism of nine task forces which have functioned since April, 1967. These Task Forces have identified a variety of problems of regional significance within their particular areas of concern. They have charted action programs to overcome some of these problems. The March, 1968 operating grant request is a composite of many of the action programs recommended by these task forces, as amplified and endorsed by the Planning Committee and the Advisory Board. Although the program's operating grant request calls for support of a number of separate projects and demonstrations, each is an integral part of a concerted course of action to develop a coordinated medical care system for Connecticut. The aims and aspirations of this program are revealed by consideration of the collective impact of the several elements of this proposal to strengthen and improve the region's capacity to deal with heart disease, cancer, stroke and related diseases—and thereby to contribute to the improvement of the whole medical care system.

On November 25, 1968 the National Advisory Council for Regional Medical Programs gave substantial endorsement to the CRMP request for operating funds by authorizing grant awards for 1969, 1970 and 1971.

In an address to a national conference on Regional Medical Programs held in Washington, D.C., on January 17, 1968, Dr. Dwight Wilbur, President-Elect of the American Medical Association emphasized what he considered the heart of the Regional Medical Programs. He stated, "The focus is on the patient; the mechanism is cooperative arrangements; the emphasis is on local initiative, flexibility and decision-making; and the reason for the program is the relationship between science and service."

It seems clear that the proposed operating program for the Connecticut Regional Medical Program embodies the very essence of these qualities.

Narcotic Addiction — The Current Problem and Treatment Approaches

Herbert D. Kleber, M.D.

In the past six years there has been an approximately twenty fold increase in the number of drug arrests both (heroin and marihuana) in the city of New Haven (see Table I). Over the last three years the number of heroin arrests alone has tripled (see Table II). Although part of this rise may reflect greater police attention to the problem, the size of the increase appears more related to the spread of narcotic addiction itself. Along with this rise in the illegal use of the so-called "hard narcotics", there has developed wide-spread use of other drugs —psychedelics (LSD, marihuana, etc.), amphetamines, barbiturates, and glue. These latter drugs have received a great deal of publicity of late, tend to be used by a different segment of the population (with the exception of marihuana), and pose hazards that although different are nonetheless real and potentially severe.¹ Because the furor attendant on the use of these "dangerous drugs" has made many lose sight of the problem of narcotic addiction which, as the above figures attest, remains a real one, the present paper will concentrate on this aspect of the current drug scene.

Nature and Extent of Problem

The relationship of the number of narcotic arrests to the actual number of narcotic addicts is unknown, whether one is speaking of local, state, or national figures. The author's professional experience in New Haven would indicate that a figure of at least twice the arrest rate would be a conservative one. Considering that the average addict uses 3 to 4 "bags" a day of heroin and that a New Haven "bag" costs \$6 (\$2 or \$3 if purchased in New York), one would also estimate that the social disorganization and petty crime secondary to addiction is much larger than just the number of addicts would indicate.

The racial breakdown of the 1964-67 heroin arrests (Table II), would suggest that in New Haven the problem with heroin addiction is mainly a Negro one. If this is the case, it would be out of line

with the figures of both the State of Connecticut as a whole (Table III) and the national figures in which only 40% of new addicts are Negro (1965 Federal Bureau of Narcotic figures). Although Negro addicts still make up somewhat over 50% of all heroin addicts, their number among new addicts has been steadily decreasing over the last 10 years.² Thus in 1956 it was 57.8%, in 1960 50.9% and in 1965 40.2%. During the same period there has been a rise among Puerto Ricans (from 7.8% to 15.7%) and among whites. Although there are no exact figures, there is a feeling also that there has been a significant rise in the number of white addicts in the suburban areas of the large cities.

The breakdown by sex shows a ratio of about 4 males to one female, on a par with national figures and almost the exact inverse of the ratio prevailing prior to the passage of the Harrison Narcotic Act in 1914.

The age factor in addiction is a significant one. The condition is most prevalent in the 20-40 age range (Table III) and after 40 there appears to be a marked diminution in the number of addicts. This phenomenon which has been called "maturing out" is still little understood but has important implications for treatment. Addiction is seen then not as a permanently incurable condition but one in which there are self-limiting features and treatment should be directed toward helping the addict live through this 20-40 age span without dying (the death rate among addicts is very high) and with a more productive kind of living. Treatment approaches to this end are discussed later in the paper.

A publication by the U.S. Department of Health, Education, and Welfare³ points out that it takes three things to make an addict: 1) An available drug; 2) a psychologically maladjusted individual; and 3) a mechanism for bringing them together. The *source* of narcotics for most New Haven addicts is New York City, and to a lesser extent Bridgeport. Because of the close physical proximity and the large price differential for drugs, a number of New Haven addicts purchase their drugs in New York, sell half on their return home, and use the rest for themselves. This type of practice obscures the difference between "pusher" and "user" that appears

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TABLE I

NARCOTIC ARRESTS IN NEW HAVEN

Year	White	Negro	Puerto Rican	Male	Female	Total	Marihuana	Heroin	Other
1961	1	4	—	5	—	5	*	*	—
1962	1	8	—	6	3	9	*	*	—
1963	19	21	—	33	7	40	*	*	—
1964	9	32	—	37	4	41	20	20	1
1965	5	46	—	48	3	51	28	23	1
1966	34	56	—	72	16	88	29	58	1
1967	63	42	4	90	19	109	65	32	12

(Jan. 1-)
(Aug. 1)

* breakdown not available

(Above figures by courtesy of New Haven Police Department Special Services Section)

TABLE II

NARCOTIC ARRESTS IN NEW HAVEN

Heroin

Year	White	Negro	Puerto Rican	Male	Female	Total
1964	—	20	—	19	1	20
1965	4	19	—	21	2	23
1966	16	42	—	46	12	58
1967	4	28	2	23	9	32

(Jan. 1-)
(Aug. 1)

Marihuana

Year	White	Negro	Puerto Rican	Male	Female	Total
1964	8	12	—	17	3	20
1965	1	27	—	27	1	28
1966	15	14	—	26	3	29
1967	47	18	2	56	9	65

(Jan. 1-)
(Aug. 1)

(Above figures by courtesy of
New Haven Police Department Special Services Section)

so clear cut when defined by law and makes the very severe legal penalties given the former often a punishment just for being an addict. Many of the addicts that the author has seen, both in New Haven and during two years at the U.S. Public Health Service Hospital in Lexington, Kentucky, have at one time or another sold drugs while using them.⁴ The non-addicted individual who is profiting from drug traffic is less often on the streets selling drugs; he is more often wholesaling or importing them instead.

The "addictive personality" appears also to be a misunderstood entity. Although there are certain personality traits that are shared by many addicts—passivity, dependency problems, inability to handle aggression—there are many addicts that do not have these traits. Diagnostically addicts run the full gamut of psychiatric nosology. Addiction appears to be a "final common pathway" with many diverse roads leading into it. One author, for example, wonders whether the potential for drug addiction doesn't exist in all of us.⁵

TABLE III

CONNECTICUT ADDICTS—USERS AND SUSPECTS

(Heroin, Marihuana, etc.)

Year	White	Negro	Puerto Rican	Male	Female	<20	21-30	>30	>40	Total
July, 1961-June, 1962						104	492	211	*	807
July, 1962-June, 1963						98	395	232	*	725
July, 1963-June, 1964	564	181	29	623	151	138	347	289	*	774
July, 1964-June, 1965	437	227	68	617	115	144	367	221	*	732
July, 1965-June, 1966	717	293	43	879	182	333		21-40 616	98	1061

* Not broken down

(Above figures by courtesy of Narcotic Control Section, Connecticut State Department of Health)

A recent classification⁴ divides addicts into 3 categories on the basis of the reasons for initial drug use: "medical" (because of pain, sickness or on a physician's order), "emotional" (because of acute stress, anxiety, depression, feelings of inadequacy or loneliness), and "social" (drugs used for kicks, pleasure, or curiosity). Interestingly enough, these groups did not differ from each other significantly on such factors as employment history, criminal record, disturbed parental relationships or family history of behavior disorders. Two other papers^{6, 7} that attempt classifications of addicts have recently called attention to the category of the "controlled" addict who, unlike the common stereotype of the addict, is able to maintain himself without continually increasing the amounts used and without resorting to criminality to obtain money. This category requires more documentation and differentiation from the more commonly seen group as well as from the occasional week-end user. The addicted health professional with a good income often appears as a controlled addict during the early months of his addiction. In many cases his addiction was preceded by alcoholism.⁸

It has long been observed that addiction is more prevalent in areas of lower socioeconomic status. Certain demographic variables have been recently noted in a follow-up study of New York addicts treated at Lexington that point up which individuals in these areas are most susceptible.⁹ These are: 1) 20% of the patients had lost their mothers before age 16 and 50% had lost their fathers by that age; 2) in 62% of the cases at least one parent came from a different culture than that of the patient, i.e., the patient was born in the United States but at least one parent was born in a foreign country or if the patient was Negro and northern born, at least one parent was born in the Southern United States. This percentage is almost double that of the 1960 U.S. Census for New York City males of similar age and race. This second generation cultural disparity may also be related to the rising incidence of white suburban drug abuse.

The *bringing together* of the addictive drug with the potential addict is another misunderstood area. Popular lore has it that this occurs via a drug pusher but in over two-thirds of the cases this does not appear to be so.¹⁰ Instead, the individual usually gets his first experience with drugs from someone he knows who is close in age to his own peer group. In the author's experience this seems to be the case in both slum areas where addiction is endemic and in prosperous suburbia where present-

ly it is less common. This "contagion" factor makes successful treatment programs doubly effective: not only is the afflicted individual helped but his removal from the addict subculture lessens the danger of the condition spreading.

Treatment

The recently (1967) passed Connecticut law on drug addiction provides a new opportunity for transferring the problem of addiction from the legal arena to a medical setting where it more properly belong and where it can be dealt with more effectively and humanely. This law comes at an opportune time for within the past few years there have been developed new methods for the treatment of narcotic addiction that look more promising in their total impact than anything in the 53 years since the passage of the Harrison Narcotic Act. These programs include Methadone maintenance,¹¹ Cyclazocine maintenance¹² and the Synanon—Day Top Village approach.¹³ The first of these involves the daily use of Methadone, a synthetic narcotic which has been used for narcotic withdrawal for many years. It is given once a day in high doses (about 100 to 150 milligrams daily). On such a dose the addict cannot get high from shooting his customary amounts of heroin and so usually ceases to try it. More important the drug craving is satisfied and the addict is able to engage in productive work and maintain more stable family relationships. It is important to note in this regard that providing vocational and educational rehabilitation or psychotherapy where indicated is as crucial as the giving of the drug. Currently such a program has existed in New Haven for the past six months and at least two more such programs elsewhere in the State are being planned. It is not clear yet how long patients will need to be maintained on drugs since the program is new.

Cyclazocine maintenance is a newer more experimental approach. The drug is a narcotic antagonist which if given to a narcotic addict will precipitate immediate and often violent withdrawal. If, however, the patient is first withdrawn from narcotics and then maintained daily on Cyclazocine, a blocking effect occurs with the result that injections of heroin or other narcotics do not produce any euphoria. Since drug craving, however, is apparently not affected, patients on this program need to have a higher level of motivation and more ego strength than those on the methadone program. It also appears to be more suitable for teen-agers whom one would be reluctant to start so young on

the methadone program. Physician and other professional addicts might also be possible candidates for this type of approach. Currently there is no program utilizing Cyclazocine in Connecticut of which the author is aware.

The Synanon—Day Top Village treatment involves the residential treatment of addicts in facilities run by ex-addicts farther along in the program. It relies on emotional re-education via constant critical scrutiny and intense involvement with ones peers as well as graduated steps of responsibility as one demonstrates capacity for it. Unlike Synanon which operates for the most part independent of mental health professionals, Day Top Village in Staten Island uses both ex-addicts and professional help where indicated. The psychiatric principles involved in both appear closely related to the Reality Therapy recently discussed by Glaser.¹⁴ Since the closing a few years ago of the Synanon House in Westport there was no facility like this in Connecticut until the recent opening of a Day Top facility in New Haven in November, 1968 under the auspices of the Connecticut Mental Health Center. Day Top appears to be more successful than Synanon in returning people to the community.

Another promising approach which is being attempted in at least three Connecticut communities involves the joint efforts of ex-addicts, health and legal professionals and ministers in efforts to both educate the community as to the nature of addiction and provide counselling and vocational rehabilitation to those already addicted. Unfortunately these efforts are often frustrated both by small budgets and the chronic relapses that often are a feature of narcotic addiction. As far as legal penalties are concerned, Valliant's study⁹ indicates that shorter periods of imprisonment combined with close supervision after discharge has a better chance of leading to abstinence than long periods of prison without such follow-up.

The best treatment of addiction or any other disease is prevention. In the light of our present knowl-

edge this would involve at least the following: improvement of the socioeconomic conditions in the slums where addiction is endemic; concentrated educational and counseling measures toward high risk groups such as siblings of addicts, children of one parent families, and the second generation teen-agers alluded to earlier; and early case finding and medical treatment rather than incarceration.

Bibliography

1. Kleber, H. D.: Prolonged Adverse Reactions From Un-supervised Use of Hallucinogenic Drugs, *J. Nerv. Ment. Dis.*, 144:308-319, 1967.
2. Schumach, M.: Decline in Negro Narcotic Addicts, *N.Y. Times*, March 6, 1967.
3. *Narcotic Drug Addiction*, Mental Health Monograph 2, U.S. Department of Health, Education, and Welfare, U.S. Government Printing Office, 1965.
4. Smith, W. G., Ellinwood, E. H. Jr., and Vaillant, G. E.: Narcotic Addicts in the Mid-1960's, *Public Health Reports* 81:403-412, 1966.
5. Laskowitz, D.: "Psychological Characteristics of the Adolescent Addict" in Harms, E., *Drug Addiction in Youth*, Long Island City, N.Y.: Pergamon Press, Inc., 1965, pp. 67-83.
6. Zinberg, N. E., and Lewis, D. C.: Narcotic Usage, *New Eng. J. Med.* 270:989-993, 1964.
7. Scher, J.: Patterns and Profiles of Addiction and Drug Abuse, *Arch. Gen. Psychiat.* 15:539-551, 1966.
8. Weech, A. A. Jr. and Kleber, H. D.: Narcotic Addiction in the Middle Class Patient, presented at the Annual Meeting of the American Psychiatric Association, Detroit, May, 1967.
9. Valliant, G. E.: A Twelve-Year Follow-Up of New York Narcotic Addicts: I. The Relation of Treatment to Outcome, *Am. J. Psychiat.* 122:727-737, 1966.
10. Chein, I., Gerard, D. L., Lee, R. S. and Rosenfeld, E.: *The Road to H*, Basic Books Inc., 1964.
11. Dole, V. P. and Nyswander, M. A.: Medical Treatment of Diacetylmorphine (Heroin) Addiction, *J.A.M.A.* 193:646-650, 1965.
12. Jaffe, J. H. and Brill, L.: Cyclazocine, A Long Acting Narcotic Antagonist: Its Voluntary Acceptance As a Treatment Modality by Narcotics Abusers, *Internat. J. Addictions* 1:99-123, 1966.
13. Yablonsky, L.: *The Tunnel Back: Synanon*, Macmillan, New York, 1965.
14. Glasser, W.: *Reality Therapy*, Harper and Row, 1965.

Air Pollution Control and Research Activities in Connecticut

J. E. Yocom

Introduction

Man is the most successful of the air-breathing animals in adapting to the stresses of his natural environment. Robert Ardrey¹ calls man the "bad-weather animal" because of his unique ability to adapt to a wide variety of primitive natural environments. Yet today the environment into which we are born and presumably thrive is no longer completely "natural." The essentially man-made environment of our congested cities is a far cry from the sylvan or pastoral surroundings of our ancestors. By and large man has taken in stride these rapidly changing conditions. However, in our heavily urbanized and industrialized centers there are indications that man is not adapting rapidly enough to the environmental changes created by his own superior intelligence and productivity.

Of the three basic necessities of life (air, water, food) air is certainly the most critical:

<i>Man's Needs</i>	<i>Pounds per day</i>	<i>Survival Time Without Each</i>
Air	30	5 minutes
Water	4.5	5 days
Food	2.75	5 weeks

Furthermore, air is the "sea around us" which we cannot easily escape and which we must accept in whatever condition it is presented to us. Water and food supplies on the other hand are easily controlled and we can either accept or reject them based upon their apparent quality. Thus the contamination of our atmosphere may be the most serious environmental problem facing man.

The quality of the air presented to residents of Connecticut varies considerably depending upon meteorological conditions. In general, the ability of the air in Connecticut to assimilate and disperse pollutants is greater than in many other parts of the country (e.g., the Los Angeles Basin). Nevertheless, under light southwest winds and with stable atmospheric conditions (a common occurrence in the Summer and Fall), pollutants can build up to significant levels in the southwestern and central

portions of the State. This condition is related both to meteorology and to the orientation of the principal urbanized areas of the State. The development of the State is a continuation of the urban area of the New York-New Jersey metropolitan region which in turn is an extension of a vast megalopolis originating in the vicinity of Washington, D.C. Thus with southwest winds much of Connecticut is exposed to both in-state and inter-state air pollution.

Within the past five years interest and activity in the field of air pollution has increased at a rapidly increasing rate. The role of Connecticut institutions in this increased concern has been significant. The following sections present a sampling of these activities. While not necessarily exhaustive, this discussion shows the diversity of work presently in progress and Connecticut's important role in improving the quality of the atmosphere.

Connecticut State Health Department

Active concern about the State's air pollution goes back to about 1958 when the State Health Department assigned a full-time man to the responsibility of air pollution control in the State. Work at this time was limited largely to answering complaints, inspecting refuse disposal sites, and working cooperatively with industries and local communities. In 1963 Connecticut law 19-30A was passed which officially recognized air pollution as a problem in the State and authorized the Health Department to establish an air pollution control function. During this same year Congress passed the Clean Air Act which, among other things, provided grants to states and local government on a matching basis (\$2 of Federal funds for each \$1 of locally developed funds) to strengthen their air pollution programs. Although the State law did not authorize specific abatement activities, the Federal grant assistance permitted the State Health Department to establish an Air Pollution Control Section and begin the important factfinding mission that is an indispensable prelude to any air pollution abatement program.

An air pollution control bill proposed in 1965 did not pass the General Assembly, but an amendment to an earlier law covering municipal incinera-

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tors was broadened to include all refuse disposal at municipal refuse disposal sites and made significant inroads on the problem of large scale open burning.

In 1967 the first major piece of legislation governing air pollution in Connecticut passed the Connecticut General Assembly—Public Law 754. This is basically an enabling act which provides for a ten-man Air Pollution Control Commission which has the authority to adopt rules and regulations for the purpose of reducing emissions of air pollutants within the State. The Commissioner of Health is empowered to enforce the regulations adopted by the Commission. In the relatively short time this Commission has been in existence regulations have been adopted which further limit open burning and which authorize the Commissioner of Health to demand reduction of pollutant emissions from certain classes of sources within the State in the event of prolonged periods of weather characterized by a high air pollution potential.

The Commission is currently considering various regulation concepts for use in controlling emissions of visible smoke and other particulate matter and is expected to adopt regulations soon on the emissions of these types of pollution.

Concurrent with the activities of the Commission, a 128-member Clean Air Task Force is considering technological, economic, legal, planning,

sociological, and many other facets of the entire air pollution problem of the State with the aim of advising the Governor on the directions which air pollution control activities should follow in the future.

The Air Pollution Control Section of the State Health Department has initiated a number of study projects to gather basic data on the nature and extent of air pollution in various parts of the State. Table 1, adopted from an article by Proulx,² is a yearly summary of air quality data from the 20-station network operated by this group with the cooperation of local health and other municipal departments. In this instance air quality is measured in terms of concentrations in air of solid particulate matter in units of micrograms per cubic meter. It is apparent from the data that maximum particulate concentrations occur in the largest and/or the most heavily industrialized cities. Since population and the associated activities of people appear to be a significant factor in determining measured levels of community air pollution, it is of interest to investigate the correlation between particulate concentrations and population for the 20 towns listed in Table 1. If one plots the simple relationship between particulate concentration and population, the extreme scatter of the points makes interpretation difficult. This scatter indicates that

TABLE 1
CONCENTRATIONS OF SUSPENDED PARTICULATE MATTER IN SEVERAL CONNECTICUT TOWNS

(State Department of Health Data for 1966)

Town	Population	Suspended particulate concentration $\mu\text{g}/\text{m}^3$				Average
		Winter (January)	Spring (April)	Summer (July)	Fall (October)	
Hartford	162,000	72	72	85	99	83
Bridgeport	155,000	113	97	101	85	99
New Haven	151,000	—	86	89	103	93
Waterbury	108,000	77	87	74	105	86
Stamford	105,000	—	79	91	108	92
New Britain	88,000	58	85	79	111	83
Greenwich	62,000	—	55	68	82	68
Fairfield	54,000	33	52	42	45	43
Danbury	47,000	38	50	74	60	56
Stratford	45,000	29	26	64	65	46
Norwich	41,000	—	45	77	69	64
New London-Groton	34,000	—	64	61	50	58
Middletown	32,000	48	59	69	40	54
Torrington	31,000	24	41	50	59	44
Thompsonville	27,000	—	—	77	87	82
Naugatuck	21,000	56	68	86	63	68
Ansonia	20,000	106	79	89	169	110
Winchester	11,000	16	46	46	77	58
Putnam	8,500	39	46	78	66	57
Thomaston	6,500	50	54	64	121	72

many factors other than population contribute to levels of this pollutant. By plotting on log-log graph paper the ratio of particulate concentration to population versus population, as shown in Figure 1, the scatter of points representing the towns is reduced and a smooth curve can be drawn through the points. Nevertheless, the scatter is in a logical pattern because most of the points below the curve (the "norm") are of an essentially residential nature (e.g., Middletown, Stratford, and Fairfield) and have a lower than "normal" ratio of particulate matter to population. By the same token, points representing towns which are significantly above the curve (e.g., Ansonia, Naugatuck and Bridgeport) have significant industrial air pollution contributions.

The Air Pollution Control Section is currently expanding this monitoring network both in number of stations and number of pollutants measured

and has plans to automate four of these stations and telemeter the data to the Hartford headquarters. Additionally, this group is developing a state-wide plan for cooperative air pollution control efforts between the State and the cities in the areas of atmospheric sampling, source inventories, abatement, information, and education.

Connecticut Research Commission

The Connecticut Research Commission was established in 1965 by the passage of Public Act No. 459. It is a tax supported agency which sponsors research in various laboratories throughout the State. The only basic limitation on the scope of research supported by the Commission is that it be able to show short term or long term benefits to the citizens of Connecticut.

Since 1966, when active sponsorship of research was initiated, three grants have been awarded for research in the field of air pollution:

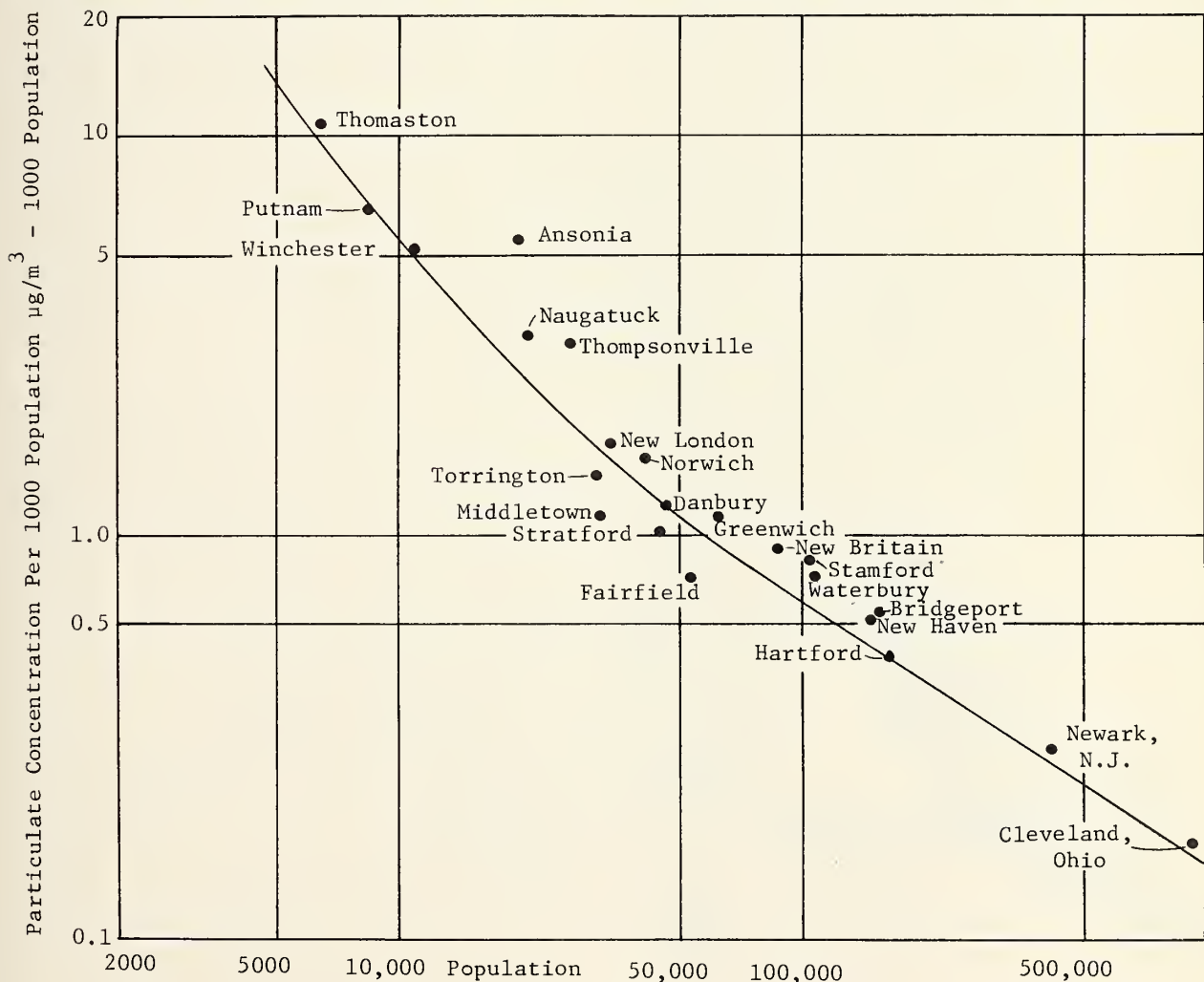


Figure 1

Particulate matter concentrations in Connecticut cities related to population (1966 data from Connecticut State Health Department).

1. "The Development of a Simulation Model for Air Pollution over Connecticut," The Travelers Research Center, Inc., G. R. Hilst, one year from October 1966.

2. "Analysis of Nitrogen Oxides by Ultraviolet Spectrophotometry," Fairfield University, J. C. McDonald, 18 months from February 1968.

3. "Venturi Type Air Pollution Control Device," University of Bridgeport, E. S. Tillman, Jr., one year from April, 1968.

The total amount of these three grants exceeds \$125,000.

The simulation model of air pollution in Connecticut developed by The Travelers Research Center, Inc. (TRC) is a mathematical statement of the air pollution "system."³ In simple terms this model describes the quantitative relationship between the sources of pollution, the meteorological conditions which transport and disperse the pollutants, and the resulting air quality in terms of the concentrations of a specific pollutant. The two principal elements of the study were the source inventory and the atmospheric diffusion models.

The source inventory consisted of piecing together bit by bit an estimate of emissions of five specific pollutants from all of the major sources within the State and displaying the data geographically in terms of 5000-foot grid squares. Without the use of high speed computers to store basic data and carry out the mathematical manipulations of the data, such a job could not have been attempted. Figure 1 shows a computer generated source map for hydrocarbon emissions. Since the principal source of hydrocarbons is the automobile, the pattern of emission is closely related to the roadway

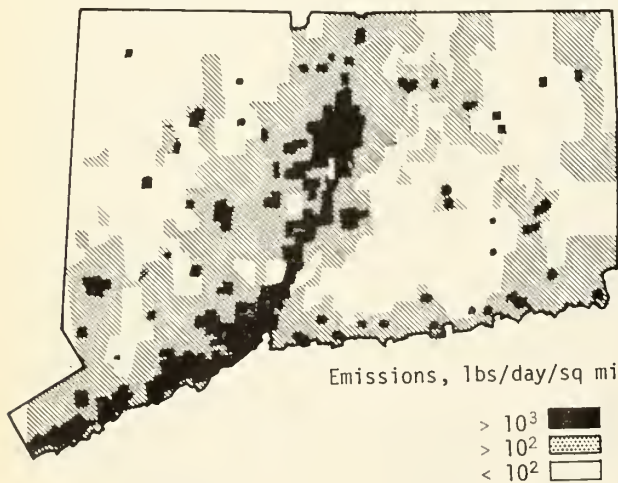


Figure 2

Pattern of average hydrocarbon emissions in Connecticut.

system in the State. In a similar manner, source emission maps were developed for other pollutants and the pattern which emerged could be related to land use responsible for the emission. For example, sulfur dioxide emissions were related closely to domestic and industrial uses of sulfur-containing fuels.

Concurrently with the source inventory, atmospheric diffusion models were being developed which represent typical weather regimes over Connecticut. These models were programmed into the computer and "told" to operate on the source data and generate maps of pollutant concentration over the entire State. Figure 3 shows a computer generated air quality map for sulfur dioxide on a typical January morning with a northwest wind blowing.

TRC is currently validating the model by means of a comprehensive field testing program. Once validated and modified, where required, to conform with actual field measurements, the model should be extremely useful to various institutions within the State. For example, air pollution control authorities, whether at the State, local, or regional level, can determine quantitatively the effect of proposed control regulations; planning regions can determine the effect of different types of land use in a given area on air quality; and industrial development groups can determine the impact of specific types of industrial development on air quality in areas adjacent to locations of proposed development.

Control Activities at the City Level

Under the provisions of the Federal Clean Air Act of 1963, a number of Connecticut cities applied for and received grants to establish or strengthen

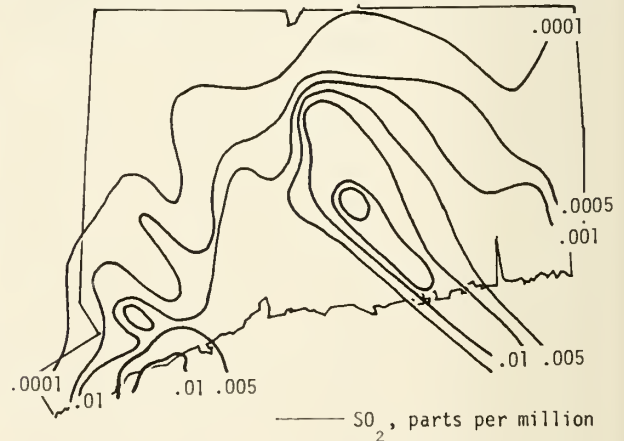


Figure 3

Predicted patterns and levels of SO_2 concentration under steady NW wind, clear skies, Connecticut sources only—for a January day, 6:00 a.m.

levels of sulfur dioxide measured during this study.

3. Based on present land use and that anticipated in the future, the level of "unacceptable" air quality will cover most of the region by the year 2000, unless vigorous action is taken now to control existing and new sources of pollution.

4. Since the problem is regional in nature, and significant sources of pollution lie outside of the Capitol Region, it was recommended that at least the towns of New Britain, Plainville, and Bristol be included in any regional effort to control air pollution.

Shortly after the issuance of this report the Central Connecticut Planning Region, which includes the three towns listed above, has stated its desire to cooperate with the Capitol Region for the purpose of regional air pollution control.

Connecticut Agricultural Experiment Station

A wide variety of vegetation is damaged by air pollution. Ozone and "photochemical smog" are the principal culprits in Connecticut. Ozone, strangely enough, is not emitted as such in any significant quantities from any particular air pollution sources. Rather, it is produced in the atmosphere in a complex series of photo-chemical reactions from other types of pollutants, notably hydrocarbons and nitrogen dioxide.

Where vegetation damage is of economic concern to agriculturists in the State, the Connecticut Agricultural Experiment Station is likewise concerned. Ozone damage to shade-grown tobacco in the Connecticut Valley has been recognized by this group since 1951. During 1959 a \$3 million loss from this source was suffered by the tobacco growers—a \$30 million business in the State. Research efforts at the experiment station on air pollution damage and methods to control it cover a wide spectrum from the fundamental to the practical. Basic research is concerned with the biochemical mechanisms of ozone injury to tobacco and other plants. Working cooperatively with the tobacco growers, studies of the genetic resistance to ozone have resulted in strains of tobacco which are relatively more resistant to ozone. Had these resistant strains not been developed, the tobacco growing industry could well have been wiped out in Connecticut. Research has also been carried out on materials which can be applied to the cloth covering for tobacco fields or to the tobacco leaves themselves which will inhibit injury.

Universities

The colleges and universities in Connecticut are becoming increasingly interested in air pollution through teaching and research. The Department of Epidemiology and Public Health of the Yale School of Medicine offers graduate courses in "Air Hygiene," "Community Air Pollution Control," "Air Sampling and Analysis," and "Air Pollution Meteorology." Current research projects are concerned with respiratory physiology and epidemiological studies in relation to air pollution. Federal grants awarded through the National Air Pollution Control Administration support a considerable portion of these activities.

The John P. Pierce Foundation laboratory, a research group affiliated with Yale University, is conducting studies to show the effects of various air pollutants (e.g., SO₂, NO₂, and O₃) on animal lung tissue. Other work by this group has been concerned with the effects on the human respiratory system of exposure to a wide variety of air contaminants encountered in workroom atmospheres.

Industrial Activities

The industrial community in Connecticut is deeply involved in the air pollution problem in the areas of research, marketing of control equipment and processes, and in the many diverse activities of those industries investigating methods for controlling their air pollution emissions. Therefore, it is not possible in an article such as this to cover all such work.

One example of industrial concerns involved in a wide variety of air pollution and research and control activities is Combustion Engineering, Inc. in Windsor. This company designs and produces heavy equipment for the power generation field. Since power generation with sulfur-containing fuels contributes heavily to emissions of sulfur oxides to the atmosphere, Combustion Engineering has been in the forefront of those developing processes for removal of SO₂ from power plant stack gases. The Combustion Engineering process consists basically of injecting dolomite (naturally occurring calcium magnesium carbonate) along with the coal or oil into a boiler and passing the exhaust gases through a water scrubber. Both SO₂ and solid particulate matter are removed at high efficiency. Full scale systems are now being tested on boilers in the mid-west and air pollution control technologists are anxiously awaiting data and information on operating experience from these units.

Other activities at Combustion Engineering include investigations on emissions of nitrogen oxides from boilers, and development of new refuse incinerators and dust collectors.

The principal power companies in Connecticut (Connecticut Light and Power Company, Hartford Electric Light Company, and United Illuminating Company) have continuing programs for minimizing emissions of pollution. Most of the fossil fuel plants have achieved a high degree of continuous control of particulate emissions. Since there are as yet no proven, feasible methods for removal of sulfur oxides from stack discharges, most plants have adopted plans to have available a supply of low sulfur fuel for use during periods of high air pollution potential.

In conjunction with these control programs, the power companies have conducted air quality and meteorological studies designed to show the effect of fossil-fuel generating stations on levels of pollutants in areas surrounding these plants.

Conclusion

From this sampling of activities it should be evident that Connecticut institutions are actively engaged in a wide spectrum of work covering Connecticut's specific air pollution problems as well

as the more general problem facing the country as a whole. It should also be apparent from the diversity of groups working on the problem that progress can be achieved in its solution—either on a statewide or national basis—only through the joint efforts of scientists, engineers, physicians, industrialists, politicians, government administrators, and citizens. Physicians have an especially important role to play in the ultimate control of the quality of our atmospheric environment. By increasing their awareness and understanding of the nature of air pollution and its effects and their participation in defining the epidemiology of air pollution, physicians will be in an excellent position to provide guidance in many areas of the problem.

References

1. Ardrey, R., *African Genesis*, Atheneum, New York 1961, 380 p.
2. Proulx, L. J., Jr., *The Rising Tide of Air Pollution*, Connecticut Health Bulletin 81, 3 (March) 1967.
3. Hilst, G. R., et al., *Final Report on the Development of a Simulation Model for Air Pollution over Connecticut*. The Travelers Research Center, Inc., Hartford, Conn., October 1967.
4. Yocom, J. E., et al., *Summary Report—Air Pollution Study of the Capitol Region*, TRC Service Corporation, Hartford, Conn., December 1967.

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The Development of Medical Education in the United States

David S. Cannom, M.D.

As long as the art of healing has been practiced it has also been taught, at first orally, later by means of written records supplemented by oral teaching. Aesculapius himself is said to have been taken to the centaur Chiron that he might teach him the ways of healing diseases which bring many woes to mankind.—Pindar Pythian Ode 3:80

The laboratory has come to furnish alike to the physician and to the surgeon on a new means for diagnosing and combating disease. The education of the medical practitioner under these changed conditions makes entirely different demands in respect to both preliminary and professional training.—Abraham Flexner, Medical Education in the United States and Canada, 1910

Specialization is a direct consequence of the fact that no man can hope to know his way about the entire range of medicine: . . . To the extent that such a state of affairs is a consequence of the structures of the Flexner Report it must be agreed that after 55 years it has had its inning. The medical school must face a new orientation as radically different as that of 1910.—O. Cope and J. Zacharias Medical Education Reconsidered, 1966

From 1606 when the first doctor landed in Jamestown with Captain John Smith to 1765 when the University of Pennsylvania Medical School was founded, a period of 150 years, there was no formal medical education in the American colonies. During this period the only method of acquiring a medical education was by the apprenticeship system. Young men of science were indentured to some reputable practitioner

“. . . to whom (the student's) service was successively menial, pharmaceutical, and professional; he ran his master's errands, washed the bottles, mixed the drugs, spread the plasters, and finally, as the stipulated term drew toward a close, actually took part in the daily practice of his preceptor—bleeding his patients, pulling their teeth, and obeying a hurried summons in the night.” (3, p. 5)

The usual length of training was three to four years and a diploma was given to the would-be practi-

tioner when his mentor thought that he was equipped to practice by himself.

The roots of this system can be traced to the way in which many British practitioners were trained between the 17th and 19th centuries. Since the 13th century, elaborate doctor-scholars had been trained by the British Universities, and, after 1518, licensed by the Royal College of Physicians. Yet other types of practitioners, the barber surgeon and the apothecary, both of whom were trained by the apprentice system, practiced alongside the university physicians, and after 1700 were called “doctors” irrespective of their lack of training. (10, p. 710) It was these men who came to the colonies, while the London university physicians did not make the Atlantic crossing, and in this way “apprenticeship played an essential role on both sides of the Atlantic.” (10, p. 710)

During the colonial era in America there was no apparent concern over the lack of training or licensing requirements of these early practitioners. The earliest known legislation intended to control the activities of practitioners was passed in Virginia in 1639, but this concerned itself with the charging of excess fees. (1, p. 695) There is no record of legal action governing the practice of medicine until 1806 when, in New York, in each country, physicians were authorized to form local societies which had the power to grant licenses. (1, 696)

In 1765 the founding of the University of Pennsylvania Medical School revolutionized American medical education. The story of this institution is really that of its first teachers, John Morgan and William Shippen. Both Shippen and Morgan, after a period of apprenticeship in Philadelphia, went to London where at Guy's and St. Thomas hospitals they saw typical hospital schools with medicine and surgery being taught on the wards. They went to Edinburgh, a university school in which instruction was given largely by lectures and where theory

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was emphasized with very limited clinical opportunities. (10, p. 711) They were exposed to William and John Hunter, and Colin Mackenzie. Shippen returned to Philadelphia before Morgan and initially opened a private school of anatomy and began a series of lectures on midwifery, which was ". . . the first systematic teaching of medical subjects at anything approaching an academic level in the American colonies." (2, p. 720) Morgan returned to Philadelphia in 1765 after a year in Paris and was made professor of the theory and practice of medicine in the College of Philadelphia. At the two day founding ceremony of the medical school on May 30-31, he read his "Discourse on the Institution of Medical Schools in America" which is a classic in its foresight. Morgan's chief points were:

1. A medical school ought to be an integral part of a college or university.
2. Hospital instruction should form an integral part of instruction in a medical school.
3. Young men should come to the study of medicine with a liberal education.
4. The curriculum should follow a graded order from anatomy to clinical instruction and experience.
5. Teachers should have time out to experiment and search for the secrets of nature.

(7, p. 715)

In a sense, events of the next 200 years of American medical education will to varying degrees be an acceptance, neglect, or repudiation of Morgan's principles. This address, as Norwood emphasizes, ". . . contained sound guide lines for the development of medicine as a university discipline without disrupting the conventional system of practical apprenticeship." (7, p. 715)

It is interesting to note that though Morgan asked for a qualified faculty under university control, thorough academic preparation, a graded curriculum, close affiliation with a hospital, and high standards for graduation, that he did not originally ask for chairs of surgery or midwifery. (2, p. 720) It is probably no accident that these areas were Shippen's specialities. Though there were differences in aim, Shippen and Morgan had in common ". . . a strong sense of the limitations of the apprentice system." (2, p. 720) It was their goal to supplement the apprentice's practical experience with his preceptors by giving formal systematic, academic lectures and imposing strict requirements for graduation.

The first University of Pennsylvania Medical School class, comprised of ten members, graduated

in June of 1768, having been taught only by Morgan and Shippen, the former lecturing on the theory of medicine, chemistry, and materia medica plus botany; the latter lecturing in anatomy and surgery. The requirements for an M.B. degree in 1768 specified one year in attendance at the Pennsylvania Hospital, which had been flourishing for ten years. The school maintained a two year graded curriculum which resembled the Edinburgh pattern.

In the fall of 1768 the chair of botany and materia medica was given to Adam Kuhn, a pupil of Linnaeus, and in 1769, Benjamin Rush became the professor of chemistry. Thomas Bond taught in the clinics and insisted on the bedside teaching of medical students because he believed that the student ". . . must Join Examples with Study before he can be sufficiently qualified to prescribe for the sick, for Language and Books alone can never give him Adequate Ideas of Diseases and the best methods of Treating them." (3, p. 4)

Lectures were held from November to March each year, and by the time of the Revolutionary War, 30 students per class were attending lectures. Before 1800, three more medical schools opened; Harvard in Cambridge, Dartmouth in Hanover, and King's College in New York, the last of which awarded the first M.D. degree in the colonies in 1770. It is estimated by Carlson that at the time of the Revolution there were 3500 practicing physicians among the 3,000,000 population of the colonies. Only 400 of this number had M.D. degrees, and, at the time of this survey, only 51 had graduated from American schools. (1, p. 696)

Shortly after the turn of the century, American medical education moved into another developmental phase, the era of the proprietary school, an era of uneven standards and lax practice that was to prompt Flexner's Report a hundred years later. Yet even through this most unsuccessful period in American medical education we see that Morgan's ideas survived in the work of Nathan Davis and William Pepper, though they were not to come to fruition until the late 19th century and the influence of William Welch at Johns Hopkins.

Most observers point to the founding of the medical department of the so-called University of Maryland in 1807 as the initiation of the era of the proprietary school. As the other faculties at this university failed to materialize, the medical school, which was under control of a state-wide medical society, came to have both educational and corporate authority and was entirely self-perpetuating. Because Maryland had no university undergirding it,

it broke the pattern established at Pennsylvania of ". . . a college of medicine (as) a branch growing out of the living university trunk." (3, p. 6) And with Maryland, American medical education was to lose its identity for a century.

This was the time of America's conquest of the West. By the 1830's, pioneers living west of the Appalachian mountains numbered 3,500,00 and represented one-third of the nation's population. Here most of the proprietary schools were formed. Because of the population growth in great urban centers as well as the expansion west, there arose an inevitable demand for more physicians, over whom no professional controls could be enforced. Between 1810 and 1840, 26 new medical schools were spawned to meet the public's need for health care. Between 1840 and 1876, 47 more schools sprang up. Though many of these institutions quickly closed, the number which did survive in 1876 was again doubled by 1910. Even many of the older schools abandoned the graded curriculum and some of the standard admission and graduation requirements and patterned themselves after these new schools, which Flexner chillingly characterized:

"These enterprises—for the most part they can be called schools or institutions only by courtesy—were frequently set up regardless of opportunity or need; in small towns as readily as in large and at times almost in the heart of the wilderness . . . Wherever and whenever the roster of titled practitioners rose above half a dozen, a medical school was likely at any moment to be precipitated. Nothing was really essential but professors . . . A hall could be cheaply rented and crude benches were inexpensive . . . occasional dissections in time supplied a skeleton—in whole or in part—and a box of odd bones. Other equipment there was practically none. The teaching was, except for a little anatomy, wholly didactic. The schools were essentially private measures, moneymaking in spirit and object. Income was simply divided among the lecturers, who reaped a rich harvest . . . No applicant who could pay his fees or sign his note was turned down. State boards were not yet in existence. The school diploma was in itself a license to practice . . . The man who had settled his tuition bill was thus practically assured of his degree, whether he had regularly attended lectures or not."

(3, pp. 6-7)

The race for chartering among medical schools led to a multiplicity of unregulated schools and shattered educational standards, and all the new schools deviated to some degree from the Morgan ideal. Norwood characterized medical education in the first half of the nineteenth century as ". . . an enlightening exhibition of the life and work of

professional men, undisciplined within and unregulated from without, while they attempted to give medical care to a rapidly expanding democracy in which ingenuity was unhampered and personal liberty was glorified." (8, p. 10)

These proprietary schools abandoned the preliminary education requirements, shortened the term of the lectures to 3-4 months, and usually, for graduation, required a two year preceptorship under the guidance of a practicing physician, plus two terms of different lectures. As the profits made by these schools were proportional to the enrollment of students, the rivalries for students often became intense and at times spilled over into personal feuds. Robinson sites an amusing story:

"A prominent professor told his colleagues, with a gleam in his eye, that he had recently shaken hands with the leading professor in a rival school and while so doing had felt the rival's radial pulse and found the artery as hard as a pipe-stem. It was not necessary to explain to his medical colleagues that their rival had but a short time to live, and this news seemed to give general satisfaction."

(9, p. 12)

Flexner suggests that it was largely financial considerations which prompted these feuds by telling the story of the professor in a soon to be defunct Louisville school who was willing to pay \$3,000 for a combined chair in physiology and gynecology because of what he termed the "reflex" value (i.e., number of lucrative referrals). Naturally this same professor objected strenuously to a later division of his professorship which assigned him only physiology, on the grounds of "failure of consideration." (3, p. 6)

During the period from 1820-1850 many American medical students and physicians migrated to Paris for study, a city which was beginning to assume new clinical importance. Its universities incorporated most successfully the scientific advances in pathology, physiology, and chemistry by reforming their medical curricula to include more laboratory and clinical training, less didactic lecturing, more extensive hospital connections, and more far reaching standards. (10, p. 711) Students did their ward work in the mornings and devoted their afternoons to lectures and dissections. Practitioners were required by the government to hold official degrees. Young Americans who had spent time in Paris returned to find no place in the American scheme for investigation and experimentation which, directly encouraged by Napoleon, was so important in France. Rather, most medical school teachers in

America made their living by practicing medicine. The small number of Americans who returned home to begin clinocopathological investigations were the exception whose impact was not felt for decades.

Yet periodic, if ineffective, efforts toward reform were made. The American Medical Association was founded in 1847, holding its first meeting in Philadelphia in 1847, where Nathan Smith Davis recommended that the following steps be taken to improve medical education:

1. That the course of lectures be prolonged from 4 to 6 months.
2. That there be sequence and grading in the curriculum.
3. That there be a separation of the licensing from the teaching function.
4. That better preliminary education requirement be instituted.

(1, p. 697)

But the A.M.A. had no legislative powers or control over the functions of the individual states and had no way to implement its resolutions. In 1852 the A.M.A. passed a resolution which stated that no college could send delegates to their meetings unless it:

1. Had six members on the faculty.
2. Gave one course of instruction annually of not less than 16 weeks in anatomy, materia medica, medicine, surgery, midwifery, and chemistry.
3. Required that the candidates for graduation be 21 years old, having studied 3 years; two with a respectable practitioner, having attended two full courses of lectures not in the same year, and having shown by examination that they were qualified to practice.

(1, p. 698)

During this period there was a striking gap between the rarefied ideals of some medical educators and the real squalor which characterized many of the education operations. Even at some of the better schools there was an astonishing amount of antipathy toward reform. A classic of its kind is the statement by Henry J. Bigelow, a professor of surgery at Harvard in 1871, who said, "It is safe to say that no successful school has thought it proper to risk large existing classes and large receipts in attempting a more thorough education." (3, p. 9)

Nonetheless, significant advances did occur, usually as the result of the formation of a new school rather than by the revision of an existing one. The University of Michigan which opened in 1850 specified advanced requirements for admission and graduation and remunerated members of its medical faculty by salaries from the university itself,

which freed them from a direct dependency upon students' fees. In 1859, under the leadership of Nathan Smith Davis, founder of the A.M.A., the Lind University Medical School was founded in Chicago with a three year graded curriculum, twelve professors, and excellent clinical facilities. Though the school closed during the Civil War, it eventually became part of Northwestern University. Also, in 1869 Charles W. Eliot became president of Harvard and took a new interest in the medical school. He attended meetings of the medical faculty and initiated a movement to grade the curriculum, to lengthen the course to three years, and to provide better facilities for clinical and laboratory teaching. However, when he suggested that written examination be given for the M.D. degree, the professor of surgery protested on the grounds that over half the students could barely write. (8, p. 468)

After the Civil War, many American physicians and students began studying in German medical centers. German medical education was decentralized into 15 to 20 independent rival schools. German professors were all well rewarded on a full time basis and their institutions provided a supreme example of the university type of medical school which was, by and large, still 40 years away in America.

Two important events during the last quarter of the 19th century presaged the eventual reform of medical education in this country. First was an address in 1877 by William Pepper who, as professor of medicine at the University of Pennsylvania, pointed the way toward a new direction in medical education. He said that the troubles affecting the medical profession had been steadily advancing for fifty years. He violently attacked the commercial spirit of medical schools, declared that the reform of medical education was being demanded both by the profession and by the public, and advocated the further development and strengthening of state boards of licensure as the practical means of correction. He argued that, "The time has come when those schools which would be true to themselves, to their alumni, and to the weighty interests entrusted to them, must make an advance in their system of education." (12, p. 198) He suggested that, in light of the chief defects of the system, the following reforms were needed:

1. The establishment of a preparatory examination.
2. The lengthening of the period of collegiate studies to at least three full years.
3. The careful grading of the courses.

4. The introduction of ample practical instruction of each student both at the bedside and in laboratories.
5. The establishment of fixed salaries for the professors, so that they may no longer have an pecuniary interest in the size of their classes.

(12, p. 199)

The second dominant influence on medical education in the late 19th century was the founding of the Johns Hopkins University School of Medicine in 1893. Johns Hopkins, a Quaker, was a successful Baltimore merchant who, in 1873, left \$7,000,000 to be used to fund the university proper and its medical school. Daniel Coit Gilman was appointed president of the university and it is he who developed the first true university graduate school in this country. (9, p. 30) We will consider the development of this school for, indirectly, by pursuing excellence, it precipitated the Flexner Report, and became the first truly modern medical school in America.

Gilman envisioned a course of undergraduate study in preparation for medical school, "Which shall train the eye, the hand and the brain for later study of medicine," (9, p. 30) and which should include a bachelor of arts degree. He was joined by John Shaw Billings, designer of the Johns Hopkins Hospital, who thought that the hospital should be the clinical center of a university school of medicine. That such thinking was not popular fifty years earlier is evidenced by an amusing story which Glaser quoted. In 1846, when the faculty of the Harvard Medical School had considered building a new school adjacent to the Massachusetts General Hospital, an inquiry was sent to the trustees of the hospital to determine their interest in this union. Their reply read:

"... in regard to the subject of building a medical college in immediate proximity to the grounds of the Hospital, they (the Trustees) cannot perceive any advantage to arise therefrom; but they think they can see that some disadvantages would be occasioned thereby."

(4, p. 1399)

Billings thought the medical school should provide the type of training which would encourage men to become original investigators. He proposed a curriculum that has a very contemporary ring to it, in which the first two years would be devoted to the medical sciences, while the whole course would take four years. This proposed course required two more years than the courses in most schools at this time. He encouraged the value of the investigative spirit in the study of patients, for "... nature's ex-

periments on the human body cannot be repeated at will, like those in comparative Physiology, and the phenomena must be observed as they chance to occur or not at all." (9, p. 34)

Gilman and Billings next sought a Faculty of Medicine. The first appointee was William Welch as professor of pathology in 1884. With the appointments of William Osler, William Halsted, and Howard Kelly, the chiefs of medicine, surgery, and gynecology and obstetrics, along with Welch, came to be known as the "Big Four" of Johns Hopkins. Years later, Welch reviewed the conditions which "... enabled us to make rather distinctive advances." (12, p. 199)

"We require, as you know, a liberal education as represented by a degree in arts and science . . . We ask (future students) to supply training in the sciences fundamental to medicine, chemistry, physics, general biology, with a reading knowledge of French or German . . . One of the great marks of progress in medical education is due to recognition of the fundamental nature of physiology study for the training of the physicians. . . The other subjects we were able to establish upon a fairly adequate basis were pathology, bacteriology, pharmacology, and physiological chemistry . . . and for the first time were adequately organized with laboratories . . . The main thing was the introduction of the English plan of teaching the fourth year students in the wards of the hospital by the system known as 'clinical clerks,' a marked advance, I believe in clinical teaching . . . The plan of the organization of the hospital, was, I think, a considerable improvement. It consisted mainly in the introduction of a higher resident staff over the interns . . . The young men devote their entire time, of course, to hospital work and are expected to undertake some investigative work . . . There is no time (for the heads of departments) to engage in outside practice . . . They can see private patients if they like but not having financial interest in seeing them, they will see only those that are of special interest to them."

(12, pp. 199-206)

The establishment of this school created precedents the implications of which took the next 60 years to explore, with no important revisions occurring until the 1950's. Norwood states that "... no 19th century medical school was so thoroughly planned or broke so completely with the domestic tradition which held American medicine in its strangling grip." (7, p. 716) Flexner wrote later that "... educational process and systems are usually of evolutionary origin. Three centuries of gradual development are responsible for present-day elementary, secondary, and college systems. But the graduate schools, research institutes, and medical schools

now flourishing in the United States are not the slow outcome of evolution; they represent an unprecedented leap. Mr. Gilman took this leap. The Johns Hopkins University . . . was an outright innovation." (11, p. 1414) No other decade in the history of American medical education was so decisive.

From the opening of the Hopkins in 1893, events moved more quickly. In 1902, the president of the American Medical Association appointed a committee to evaluate the A.M.A.'s role in elevating educational standards. From this, the Council on Medical Education was established in 1904. It was this council which desired professional assistance and contracted the Carnegie Foundation to play the sponsoring role for a survey of all medical schools in the country.

The result of the Carnegie Foundation investigation was published in 1910, and entitled *Medical Education in the United States and Canada*, or the Flexner Report. This legendary document—brutally frank and remarkably foresighted—must be put in proper context. The Flexner Report did not revolutionize medical education by itself but gave impetus and prominence to movements in medical education that had existed for at least four decades. Many of these achievements have already been mentioned: Charles Eliot's reforms at Harvard (1870), the opening of Johns Hopkins (1893), and the reconstruction of the American Medical Association (1910). There were other less newsworthy events which became significant in portraying trends: the opening of the first university hospital at the University of Michigan (1869); the establishment of state boards of medical examination and licensure; reports on medical education by John H. Rauch of the Illinois State Board of Health (1877-1891); the formation of the Association of American Medical Colleges (1890). (6, p. 340); and the establishment of the pathology laboratory at Bellevue by William Welch (1878). But in the period from 1876 to 1900 alone some eighty new schools opened their doors. So though gaining strength, the reform movement did not yet have enough force to counter the continuing proliferation of medical schools.

Abraham Flexner, who attended Johns Hopkins University under Gilman and then went into education, made personal visits to each of the 155 medical schools in the United States and Canada in 1909. His report, published as Bulletin Number Four, tripped the guillotine on the collective necks of the proprietary schools.

Flexner found that the country was abundantly supplied with medical practitioners. While this

country had one physician for every 568 persons, Germany had only one physician per 2,000 people. Flexner called for a drastic reduction in the number of medical schools, from 148 to 31, representing an annual output of about 2,000 physicians. He first addressed himself to the number of doctors needed: "It appears, then, that the country needs fewer and better doctors; and that the way to get them is to produce fewer. To support all or most present schools at the higher level would be wasteful, even if it were not impracticable; for they cannot be manned." (3, p. 17) His solution was as follows:

"To bring about the proposed reconstruction, some 120 schools have been apparently wiped off the map. As a matter of fact, our procedure is far less radical than would thus appear. Of the 120 schools that disappear, 37 are already negligible, for they contain less than 50 students apiece . . . Of the 120 schools, 66 are so small that their student bodies can, in so far as they are worthy, be swept into strong institutions without seriously stretching their present enrollment." (3, p. 151)

He added that these remaining schools, with few exceptions, would be departments of universities and that not more than one would be located in any one city. By 1914, four years after the report, the number of medical schools had dropped from 160 to 102. By 1918 the number was 95. At present there are 84 four year schools with four others supporting less than four year programs.

While much of Flexner's report deals with quantities, the major importance of his report rests in his comments on the quality of medical education. He addressed himself specifically to admission requirements. Of the 116 regular medical schools that Flexner visited, only 16 required two or more years of academic work as a prerequisite to admission. Some 9 schools were in the process of raising their admission requirements, while another group of 50 schools required high school graduation or an ill-defined equivalent. The remaining schools, which numbered about 40, had virtually no entrance requirements. Though not making specific recommendations, Flexner's position was clear:

"A medical school may, the law permitting eschew clinics and laboratories, cling to the didactic type of instruction, and arrange its dates so as not to conflict with seed time and harvest; or it may equip laboratories, develop a dispensary, and annex a hospital, pitching its entrance requirements on a basis in keeping with its opportunities and pretensions. . . It cannot provide laboratory and bedside instruction on the one hand and admit crude untrained boys on the other. The combination is at once illogical and future. (3, p. 22) . . .

By the very nature of the case, admission to a really modern medical school at the very least depends on a competent knowledge of chemistry, biology, and physics." (3, p. 25)

In 1905, the Council on Medical Education set one year of study devoted to physics, chemistry, and biology, as the ideal prerequisite. But they temporized by reducing the requirement to four years of high school until a time when more students would be able to qualify for the ideal requirement. While in 1904 only 2.5% of the medical schools had any college work at all as a prerequisite, by 1918, only eight years after Flexner's report, 92.2% of the medical schools required at least two years of college.

Flexner dealt with the ideal medical school curriculum in considerably more detail in his report, and it is here that his influence is still most strongly felt. It is fascinating to note how closely most medical schools have stayed with his formula. Flexner stated:

"In general, the four-year curriculum falls into two fairly equal sections; the first two years are devoted mainly to laboratory sciences—*anatomy, physiology, pharmacology, pathology.* (footnote: An introductory course in physical diagnosis is given in the second year) The last two (are devoted) to clinical work in medicine, surgery, and obstetrics. (3, p. 57) (In the third year) . . . the classes are divided into small rotating sections, each with regular appointments in every one of the dispensary departments . . . The student is trained at once to take the patient's history, to make the physical examination, to examine blood, sputum, etc., and on the basis of all the facts thus amassed to make a diagnosis and suggest a course of treatment. (3, p. 96) The fourth year is spent in the hospital under precisely the same conditions. The class is again broken into small groups. Each student gets by assignment a succession of cases . . . His 'beds' are under his continuous observation from the day his 'patient' is admitted until the day of discharge:

Meanwhile, the clinical teaching has closely followed the development of the case. At every point he has been checked up. (3, pp. 96-97) . . . The demonstrative method must, for lack of time, also be widely used. (3, p. 97) . . . even the didactic lecture may not perhaps be wholly dispensed with. (3, p. 98) . . . The class in medicine has another use; it may be made the means of training students to use the 'literature' once more, of course, only by way of amplifying an actual sense-experience. (3, p. 99) There comes a time indeed in a physician's development when any opportunity to look on is helpful; but only after he is trained; his training he cannot get by looking on. That he gets by doing; in the medical school if he can. (3, p. 100) But there is no inherent reason

why a professor of medicine should not make something of the financial sacrifice that the professor of physics makes: both give up something—less and less, let us hope, as time goes on—in order to teach and investigate." (3, p. 100)

These extensive quotes capture the spirit of reform at that time, and point out sharply that most medical schools are still in the Flexner era.

Flexner thought that all medical schools should be parts of universities. He foresaw an expansion of the concept of postgraduate education. While postgraduate courses previously had been undergraduate repair shops, providing the recent graduate with some practical techniques which the medical school had failed to teach, Flexner saw that graduate instruction should be advanced and intensive, "the natural prolongation of the elective courses now coming into the vogue." (3, p. 176)

Flexner visited each of the country's medical schools and included a summary of each in his book. He found the Birmingham Medical College to be a "stock company paying annual dividends of 6%; the hospital given over largely to surgical patients with gun-shot and other wounds;" (11, p. 1415). Of the College of Eclectic Medicine and Surgery in Georgia he said, "Nothing more disgraceful calling itself a Medical School can be found anywhere." (3, p. 205). Flexner wrote of the St. Louis College of Physicians and Surgeons the following:

Entrance requirements: Nominal

Laboratory facilities: The school occupies a badly kept building, the inner walls covered with huge advertisements. A single ordinary laboratory is provided for chemistry; there is a make-believe laboratory for experimental physiology . . . the dust-covered tables do not indicate use . . . The 'museum' consists of some cheap photographs and drawings and a few badly preserved wet specimens.

Clinical facilities: A small poorly lighted, badly ventilated, and over-crowded hospital is part of the school building . . . The school is one of the worst in the country. (3, p. 256)

In a very interesting document, this school brought suit against Flexner for \$100,000, as they had "built up a good reputation and standing throughout the country as a well-equipped medical college and (are) well-equipped and fitted to carry on its said business as a college in which is taught the science of medicine and surgery: that the good will and reputation of the plaintiff in its said business as aforesaid is of great value." (5, p. 5) After filing suit, this medical school which Flexner called

“utterly wretched” dropped the charges and was soon out of business.

It is clear that the Flexner Report proved to be the catalyst which forced medical education to become as modern as the scientific inquiry that was going on in laboratories in Europe and the United States. As Flexner noted, medicine had passed from the era of dogma, based on the teachings of Hippocrates and Galen, whose writings were transmitted as authoritative canon, through the era of the empiric which began with the introduction of anatomy in the sixteenth century and was based upon therapeutic measures usually deduced from purely metaphysical assumptions (the “art” of medicine) and had come into a third era dominated by the knowledge that a “medicine is part and parcel of modern science.” (3, p. 53) Pritchard enlarged upon this concept:

“The fundamental sciences upon which medicine depends have been greatly extended. The laboratory has come to furnish alike to the physician and to the surgeon a new means for combating disease. The education of the medical practitioner under these changed conditions makes entirely different demands in respect to both preliminary and professional training.” (3, p. vii)

Pritchard, in the introduction to the Flexner Report, clearly stated the methods by which he thought change would occur. First, he wanted to create a public opinion which would discriminate between the types of training doctors could and did receive. He wanted laws which would “require all practitioners of medicine . . . to ground themselves in the fundamentals upon which medical science rests.” (3, p. xiii) Finally, he hoped for a changed attitude of the members of the medical profession towards the standards of their own practice. As Pritchard states, “the last two factors are moral rather than education.” (3, p. xiii)

The reasons for the amazing reform of medical education after the Flexner Report are not entirely clear. The reasons are, no doubt, buried in the transitions that American society was undergoing during these decades. This was the era of the early temperance agitation, the revelations of Upton Sinclair, the trust-busting of Theodore Roosevelt. It was understood that free citizens should reform the evils of society. So when the A.M.A. and A.A.M.C. undertook reforms they were acting in accord with a national inclination. The role of government intervention was limited chiefly to the state level and included setting the provisions for licensure and the development of the state universities. As Jarcho

emphasizes, the change was accomplished by repeated, systematic collections of data and by continuous publicity. (6, p. 343)

The aim of the Flexner Report was to establish medicine on a firm scientific basis and to achieve a uniformity of standard among the country’s medical schools. The fact that most medical school curricula in the 1960’s conform, even 50 years later, remarkably closely to the Flexnerian ideal is but one measure of the report’s influence. But it is from these twin goals of scientific respectability and uniformity of curricula that the challenges to this generation’s medical educators arises.

Medicine in the 1960’s has entered upon another period of introspection, the results of which will have as precedent shattering effects as the Flexner Report had 55 years ago. While the Flexner Report was written by a professional educator and not a physician its main focus was on currents within the profession. However, the challenges of the 1960’s are arising from the interface of medicine and society as the focus shifts from medicine’s scientific underpinnings to the delivery of the advances to an increasingly sophisticated and demanding public. And while the quest of the Flexner Report was for uniformity of standards, it is this very inflexibility of curricula today which does not allow for varied responses to these new societal and scientific currents.

Since the inadequacies of the Flexner era are more easily recognizable as compared with the complex, multi-dimensional problems of contemporary American medicine, no one report will have the effect on medical education that Flexner’s did. But a revolution as profound is needed if American medicine is to respond to the challenges imposed by its having come of age scientifically.

Bibliography

1. Carlson, R. I.: The Historical Development of Medical Education in the United States. *Surgery*. 47:695-702, April, 1960.
2. Corner, George W.: Beginnings of Medical Education in Philadelphia 1765-1766. *JAMA*. 194:719-721, 1965.
3. Flexner, Abraham: *Medical Education in the United States and Canada*. New York, Carnegie Foundation for the Advancement of Teaching, Bulletin #4, 1910.
4. Glaser, Robert J.: Medical Care, Education, and Research: The Medical School and the Teaching Hospital. *New Eng. J. Med.* 271:1398-1403, 1964.
5. Jarcho, Saul: Abraham Flexner’s Lawsuit. *The Academy Bookman*. 18:3-6, 1965.
6. Jarcho, Saul: Medical Education in the United States 1910-1956. *J. of Mt. Sinai Hospital*. 26:339-385, 1959.
7. Norwood, W. F.: Critical Incidents in the Shaping of

Medical Education in the United States. *J.A.M.A.* 194:715-718. November, 1965.

8. Norwood, W. F.: *Medical Education in the United States Before the Civil War*. Philadelphia, University of Pennsylvania Press, 1944. 487 pp.

9. Robinson, George C.: *Adventures in Medical Education*. Cambridge, Harvard University Press, 1957. 338 pp.

10. Shyrock, Richard H.: European Backgrounds of American Medical Education. (1600-1900) *J.A.M.A.* 194:709-714. 1965.

11. Strauss, L. L.: Lasting Ideals of Abraham Flexner. *J.A.M.A.* 173:1413-1416. July 30, 1960.

12. Wartman, W. B.: *Medical Teaching in Western Civilization*. Chicago, Year Book, 1961. 307 pp.

PARTICIPATION BY PHYSICIANS IN BANK CARD PROGRAMS

Opinion Of The AMA Judicial Council

November 26, 1966

The growth and development of credit cards is burgeoning. A new form of card, the so-called *bank card*, is being widely introduced. Bank cards are issued without cost to the cardholder; they are acceptable at many more places than conventional credit cards; they are sponsored by large, reputable banks.

They are an innovation in our economic system.

As these bank card plans have come into being, in all parts of the country, physicians have asked if they may ethically use bank cards as a form of payment for professional services. Some medical societies have said physicians may participate; others have said physicians may not.

The Judicial Council believes a uniformity of opinion is desirable. In matters of ethics it would seem indisputable that a general rule should be determined for the guidance of the profession, and that this rule should be implemented at local level.

The medical profession has officially recognized that it cannot dictate to patients how they shall finance their medical bills. It can and should, however, determine principles to guide its members in determining whether and how they may participate in any payment program.

If the bank card were merely a substitute for cash or check in the payment of bills, little or no problem would be presented to physicians regarding their use; they would be merely a newly adopted medium of exchange. Bank cards, however, serve a twofold function: They are a convenience—a substitute for currency or check in the payment of indebtedness; and they are also a financing mechanism. Consequently, their indiscriminate use, especially the financing of larger medical bills through banks, could result in additional cost to patients. While the doctor's fee for medical care would not

increase, the cost of financing payment of that fee through a third party would be imposed on the patient. Of course, patients may voluntarily elect to pay larger amounts in return for the convenience of a given program. Still, the medical profession has a responsibility to guard against patients being placed in untenable financial conditions because of overall medical care costs. That is why medicine has been in the forefront in encouraging prepayment and insurance programs to provide for the costs of medical services. It must, therefore, maintain its position of safeguarding patients interests when considering new methods of financing personal indebtedness.

The Judicial Council is of the opinion that neither endorsement nor disapproval should be given to the bank card system at this time.

In June, 1965, the Judicial Council and the Council on Medical Service jointly agreed that any proposed plan for financing medical care or parts of medical care should be judged by the physician in the light of whether or not it might "result in advertising or solicitation of patients by physicians, profit to physicians for other than professional service, exploitation of the patient, or unnecessary increase in the cost of medical care."

Judged by these criteria, the Judicial Council is of the opinion, at this time, that physician participation in bank card programs is not per se unethical. It is of the opinion that physicians may ethically accept bank cards in the payment of current medical bills in lieu of cash or check, that is, as a medium of exchange.

The use of bank cards in financing medical fees must, however, be viewed with reserve at the present

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MEETINGS

GENERAL

March 27
185th Annual Meeting, New Haven County Medical Association

Waverly Inn, Cheshire

Business Meeting 3:00 P.M.; Dinner 7:00 P.M.

April 9
177th Annual Meeting, Hartford County Medical Association

Hartford Hilton Hotel

Business Meeting 5:00 P.M.; Reception 6:45 P.M.;
Dinner 7:00 P.M.

Speaker, Norman Cousins, Editor, Saturday Review

April 15
177th Annual Meeting Fairfield County Medical Association

Frederick's, Fairfield

Business Meeting 4:30; Reception and Dinner
7:00 P.M.

May 13, 14, 15

177th Annual Meeting, Connecticut State Medical Society

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospitals Auditorium,
New London

March 11 7:15 P.M.

Myocardial Circulation

Richard H. Gorlin, M.D., Senior in Medicine and
Director of Cardiovascular Research, Peter Bent
Brigham Hospital

March 25 7:15 P.M.

Electrophysiology of the Heart

Michael Klein, M.D., Senior Research Associate,
Peter Bent Brigham Hospital

CANCER

Oncology

Sponsored by the Connecticut Division of the
American Cancer Society and the Yale School of
Medicine. Speakers; Yale School of Medicine

Russ Home Conference Room, Griffin Hospital,
Derby

March 4 8:00 A.M.-9:00 A.M.

Tumors that Secrete Vasoactive Amines

Robert Levins, M.D., Assistant Professor of Medi-
cine and Pharmacology

March 11 8:00 A.M.-9:00 A.M.
Dermatologic Manifestations of Malignancy

Irwin Braverman, M.D., Associate Professor of
Dermatology

April 1 8:00 A.M.-9:00 A.M.

Management of Patients with Lymphoma

Ronald DeConti, M.D., Assistant Professor of Medi-
cine and Pharmacology

Chairman, Doctor DeConti; Co-Ordinator, Vincent
A. Deluca, Jr., M.D., Assistant Clinical Professor
of Medicine

Open to all physicians

May 8-10

National Conference on Breast Cancer

Shoreham Hotel, Washington, D.C.

Sponsored by: American Cancer Society, Cancer
Control Program, U.S. Public Health Service. A
multidisciplinary review of the breast problem
in the U.S. will be present, including epidimi-
ology, etology, detection, diagnosis, management
and central measures.

No registration; preregistration required

MEDICINE

Pulmonary Diseases and Pulmonary Physiology

Wednesdays 12:00 P.M.-1:15 P.M.

Radiation Center Conference Room, Hospital of
St. Raphael, New Haven

Chairman: John B. Berte, M.D., Director, Depart-
ment of Pulmonary Diseases and Inhalation Ther-
apy, Hospital of St. Raphael

Open to all physicians

Hematology

Thursdays 1:30 P.M.-3:30 P.M.

Hematology Laboratory and Wards, Hospital of St.
Raphael, New Haven

Robert P. Zanes, Jr., M. D., Hospital of St. Raphael
Open to all physicians

GENERAL MEDICINE

March 5 9:30 A.M.-4:00 P.M.

Symposium on Automobile Accidents and Trauma

Mary S. Harkness Memorial Auditorium


Yale School of Medicine

Sponsored by the Departments of Pathology and
Surgery, Yale School of Medicine

Speakers: Allen Moritz, M.D., Provost of Medical
Affairs, Case-Western Reserve University; John

(continued on p. 137)





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reserpine U.S.P. 0.25 mg.

Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.

Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs.

Use in pregnancy: Because chlorthalidone may cross the placental barrier and appear in cord blood and thiazides may appear in breast milk, this drug should be used with care in pregnant patients and nursing mothers. When used in women of childbearing age, the potential benefits of the drug should be weighed against the possible hazards to the fetus. Use of chlorthalidone may result in fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to

reserpine-treated mothers.

Precautions: Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, the drug should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Severe salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute

gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angitis are possible.

Average Dosage: One tablet daily with breakfast.

Availability: Pink, single-scored tablets in bottles of 100 and 1000. (B)46-600-C

For details, please see complete prescribing information.

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Meetings, (continued from p. 133)

H. Davis, M.D., Department of Surgery, Case-Western Reserve University; Paul Gikas, M.D., Department of Pathology, University of Michigan Medical School; Colonel John R. Stapp, U.S. Air Force Medical Corps, National Highway Safety Bureau.

Contact: Michael Kashgarian, M.D., Department of Pathology, Kristaps J. Keggi, M.D., Department of Surgery, Yale School of Medicine

No registration fee, open to all physicians

March 17-28

Clinical Management and Control of Tuberculosis
Battey State Hospital, Rome, Georgia

Sponsored by the National Communicable Disease Center

Information: No Tuition fee; Public Health Service funds are available to pay travel and subsistence expenses for a limited number of participants in each course. Attendance limited. Applications considered in order received.

Credit: Post-graduate credit given by the American Academy of General Practice. Course approved by The AMA Council on Medical Education. Future sessions scheduled for May 5-16, July 21-August 1, October 6-17, December 1-12.

Address applications to National Communicable Disease Center, Atlanta, Ga. 30333; Attn. Chief, Training Unit, Tuberculosis Program.

March 28-29

The 3rd National Congress on the Socio-Economics of Health Care

Palmer House, Chicago

Sponsored by the American Medical Association

No registration fee

April 24, 25, 26

30th Annual Session of the American Academy of Physical Medicine and Rehabilitation

Palmer House, Chicago

PSYCHIATRY

Seminars sponsored by the Connecticut Valley Hospital, Middletown; meetings held in Merritt Hall Auditorium

Visiting Faculty: Connecticut Postgraduate Seminar
March 8 2:00 P.M.

Homosexuality, Paranoia and Alcoholism

Austin McCawley, M.D.

Chairman: Iago Galdston, M.D., Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology, c/o Fairfield Hills Hospital, Newtown; Sal A. Prins, M.D., Director of Training, Connecticut Valley Hospital

Bank Card Programs (continued from p. 132)

stage of their development. While patients may not be denied the right to determine matters of their personal budgeting, physicians must not encourage the use of this financing method if in operation it might compromise the ideals of the medical profession or add to the financial burden of patients.

In connection with physician participation in bank card programs, the Judicial Council recommends the following principles to be implemented and applied as necessary by the County medical society for the guidance of physicians as these programs develop.

1. The county medical society should be satisfied as to the financial and professional integrity of the plan. It should negotiate with the plan sponsors to insure that service charges to the physician are reasonable. It should insist that the plan be open to all physicians on the same terms and that it not exploit or capitalize on physicians' participation in the plan. It should advise the plan that the listing of physicians in directories of participating members is contrary to the ethics of the medical profession.
2. The individual physician may not, because of his participation, increase his fee for medical service rendered the patient. He may not use the plan to solicit patients. He may not encourage patients to use the plan. His position must be that he accepts the plan as a convenience to patients who desire to use it. Plaques or other devices indicating participation in the plan within the physician's office shall be kept to a discreet and dignified minimum. Plaques, signs, or other devices indicating such participation visible outside the physician's office are unacceptable.
3. The use of a bank card in connection with the payment of larger fees—which might normally be paid to the physician in installments—is not to be encouraged. All members of the Association are expected to continue the traditional practice of permitting patients of limited means to pay relatively large fees in installments without interest or carrying charges. Out of respect for the dignity and traditions of the medical profession, the physician may not relieve himself of his obligations "to render service to humanity, reward or financial gain being a subordinate consideration."

OBITUARIES

Max Caplan, M.D.
1906-1968

Dr. Max Caplan of Meriden died in Lisbon, Portugal on December 6, 1968 of coronary artery disease.



Born in June, 1906 in New Haven, Connecticut, he was a graduate of Yale University in 1929 and the University of Louisville School of Medicine in 1933. He interned at Louisville City Hospital and trained in internal medicine and gastroenterology at the Montefiore and Mount Sinai Hospitals in New York City. He practiced Internal Medicine and Gastroenterology in Meriden until the time of his death. Dr. Caplan was former Chief of Medicine at the Meriden Hospital, past Chief of Staff at the World War II Veterans Memorial Hospital, Consultant in Gastroenterology at the Rocky Hill Veterans Hospital and the Bradley Memorial Hospital in Southington. He was an assistant clinical professor of medicine at Yale University.

He was certified in medicine and gastroenterology by the American Board of Internal Medicine and was a Fellow of the American College of Physicians and a Fellow of the American College of Gastroenterology.

Dr. Caplan was a past president of the New Haven County Medical Association. He was an AMA delegate and Vice-President of the Connecticut State Medical Society at the time of his death.

In addition to the numerous professional organizations to which he gave his time so freely, Dr. Caplan was also a past lieutenant governor of

Kiwanis and a tireless worker on the Meriden Library Board, and Chairman of the Meriden-Wallingford-Southington Committee for Hire The Handicapped.

Physician, Friend, Humanitarian, his devotion to and motivation for his many obligations were a source of constant inspiration to those who knew him. He leaves his wife, Evelyn, and a brother, Dr. Henry Caplan, three nephews and six nieces.

Harvey L. Fritz, M.D.

Anthony F. Massa, M.D.
1896-1968

Dr. Anthony F. Massa died suddenly on December 10, 1968 in Yale-New Haven Hospital.

Dr. Massa was born in New Haven son of the late Anthony F. and Louise Caggiano Massa. He attended St. John's and Hillhouse High School. He graduated from Yale and the Yale Medical School. Dr. Massa interned in New Haven Hospital from 1918 to 1919 and in Hartford Hospital from 1919 to 1920. He conducted his general practice of medicine in New Haven for over 40 years and was the medical examiner for the Metropolitan Life Insurance Co. and the Vocational Rehabilitation Center. Dr. Massa was a member of the American Medical Association, the Connecticut State Medical Society and the New Haven Medical Association.

He was a quiet unassuming physician who did his day's work without fanfare and will be greatly missed.

His wife Maria Giamarino Massa and a daughter Nancy, a French teacher in the Day Prospect Hill School are his immediate survivors.

Albert J. Howard, M.D.

In Memoriam

Boisvert, Paul L., Orange, University of Rochester Medical School, 1934. Dr. Boisvert was a well known pediatrician in Orange for many years. He was professor of pediatrics at the Yale School of Medicine as well as serving as physician for the New Haven Health Department. Dr. Boisvert was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the Arthritis Foundation, the American Pediatrics Society, and the American

Heart Association. He was the author of numerous articles on streptococcal infections and rheumatic fever and was a contributor to the Encyclopedia of Science and Technology, consultant to the Secretary of War and was a member of the Commission on Hemolytic Streptococcal Infections. Dr. Boisvert died December 19 at the age of 61.

Calverley, Eleanor T., Hartford, Woman's Medical College of Pennsylvania, 1908. Dr. Calverley was a general practitioner in the Hartford area for over 40 years. She was on the courtesy staff of Hartford Hospital, St. Francis Hospital, and Mt. Sinai Hospital. She was a member of the Hartford Medical Society, the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Calverley died December 22 at the age of 82.

Carbone, William C., Hamden, Georgetown University School of Medicine, 1933. Dr. Carbone was a general practitioner for over 30 years. He was on the courtesy staff of the St. Raphael's and Yale New Haven Hospitals. He was a member of the New Haven City Medical Society, the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Carbone died December 28 at the age of 58.

DellaPietra, Alphonse, Middlebury, Georgetown University School of Medicine, 1941. Dr. DellaPietra was a well-known orthopedic surgeon and chief of staff at St. Mary's Hospital, Waterbury. Dr. DellaPietra conducted a clinic in Middlebury and was influential in getting a rehabilitation center established in Waterbury. He taught for a time at New York Medical College and conducted clinics in Jordan and Brazil. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. DellaPietra died January 6, at the age of 51.

Haliday, Earle G.—Stonington, Queens University School of Medicine, Kingston, Canada—1927. Dr. Haliday was a general practitioner in the Stonington area for over 30 years. He was a member of the New London County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Haliday died December 31, at the age of 65.

Maslak, Rudolph—Warehouse Point; University of Louisville Medical School, 1934. Dr. Maslak was a well-known practicing physician in the Warehouse Point area for many years. He was a former Medi-

cal Examiner in East Windsor. Dr. Maslak was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Academy of General Practice. Dr. Maslak died October 30, at the age of 67.

Vogel, Frank S., Bristol, University of Vienna Medical School, 1927. Dr. Vogel was a general practitioner in the Bristol area for over 20 years and was associated with Bristol Hospital. He was a member of the Hartford County Medical Association and the Connecticut State Medical Society. Dr. Vogel died January 1, at the age of 67.

Cuts in Research Funds

The federal government should take "short-term corrective action" to offset the critical effects of the cutbacks in federal funds for scientific research and education, the New York Academy of Sciences says in a special evaluation of federal support.

The report, entitled "The Crisis Facing American Science," summarizes the results of a nationwide survey of 84 academic institutions and a random sampling of the Academy's 20,000 American members.

The report says reduced federal support is holding up the pursuit of potential solutions to what it calls the most pressing problems of modern society, including poverty, racial discrimination, mental illness, and cancer.

Low Morale: Minoru Tsutsui, PhD., ScD, of New York U., Bronx, N.Y. chairman of the committee which prepared the report, said that as a result of the cutbacks and other factors morale in the scientific community is low. Many scientists and engineers in colleges, universities and research centers are disturbed and soundings of scientists in private industry show they are equally concerned, he said.

The committee makes these recommendations:

- Short-term corrective action by the federal government to offset the short-term effects of the cutbacks
- Establishment of an annual growth rate of 15% for federal spending on scientific research.
- Establishment of improved methods of consultation and communication between the federal government and the scientific community.
- Determination of the federal research budget on a long-term multi-year basis.

Placement Opportunities

PEDIATRICIAN — Three member partnership in Obstetrics and Gynecology is looking for a pediatrician for the Enfield, Connecticut area, which serves a population of 60,000. An office is immediately available in a new air-conditioned medical building.

WANTED: PSYCHIATRIST—Opportunities exist in State Welfare Department for (1) a Psychiatrist to administer and coordinate the Mental Health Program; (2) Psychiatrists to act as District Welfare Department Consultants for the Mental Health Care Program. Contact: Orvan W. Hess, M.D., Medical Director, State Welfare Department, 1000 Asylum Avenue, Hartford, Connecticut 06115.

G.P. — Office space available with established physician, general practice, spending half-time writing. Association and eventual partnership. Excellent schools and municipal facilities. Fairfield County.

EDUCATIONAL OPPORTUNITY—One year psychiatric residency at 3rd year level for year beginning July, 1969. AMA approved. Unique opportunity to prepare for private practice and community psychiatry. Supervised intensive, dynamically oriented psychotherapy emphasized. Experience is meaningful application of psychopharmacological agents and somatotherapy. Work with adults and children in residential and out-patient setting. Stipend \$15,000 per annum, with major medical insurance benefits. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

EDUCATIONAL OPPORTUNITY — Investigate Rehabilitation Medicine. Young specialty with wide opportunities in teaching, research and clinical care of ever-increasing number of physically handicapped. Rehabilitation specialists diagnose and manage disorders of function, primarily chronic disorders of neuro-musculoskeletal system such as amputations, paraplegia, arthritis, strokes and cerebral palsy. In addition to using conventional medical or surgical treatment, rehabilitation management aims to develop each patient's residual abilities to optimal levels through prescription of appropriate combination of medical and physical therapy, mechanical devices, practical self-care and occupational skills, vocational skills, vocational retraining, psychological support and social readjustment. For further information, write, Robert C. Darling, M.D., Chairman, Department of Rehabilitation Medicine,

College of Physicians & Surgeons, 630 West 168th Street, New York, New York 10032.

PHYSICIANS WANTED — Two general surgeons and one internist for two years overseas assignment. Board certified, over 35, salary and related benefits. One surgeon required for service in Caribbean area available immediately; surgeon and internist for Afghanistan July, 1969. Interested parties contact MEDICO, a Service of CARE, 660 First Avenue, New York 10016, phone (212) 686-3110.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Wanted

OTOLARYNGOLOGIST — Board eligible, will finish residency June 30. Military obligations complete, desires practice opportunity.

INTERNIST — subspecialty in Infectious Diseases, recently completed residency. Desires association or group practice.

SURGEON — 38 years old, Board certified, Connecticut license. Presently in military service, but desires to terminate active duty because of increasing administrative work and wish to be in direct care of patients. Available immediately.

PEDIATRICIAN — 32 years of age, military obligations completed, Board eligible. Would like to join one or more pediatricians in any area of Connecticut. Available April 1, 1969.

PATHOLOGIST — age 43, Board certified A.P.-C.P., wishes partnership or associate position in a smaller hospital in N.E. or Central Connecticut preferably. Connecticut license.

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For coughs of colds and "flu"

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Each 5 cc. contains:
Glyceryl guaiacolate 100 mg.
Alcohol, 3.5%

For unproductive allergic coughs

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Glyceryl guaiacolate 100 mg.
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(warning: may be habit forming)
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Non-narcotic for 6-8 hour cough control

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Alcohol, 1.4%

Clears sinuses and nasal stuffiness as it relieves cough

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Each 5 cc. contains:
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Phenylephrine hydrochloride 10.0 mg.
Alcohol, 1.4%

	ROBITUSSIN	ROBITUSSIN A-C	ROBITUSSIN-DM	ROBITUSSIN-PE
EXPECTORANT	●	●	●	●
DEMULCENT	●	●	●	●
COUGH SUPPRESSANT		●	●	
ANTIHISTAMINE		●		
LONG-ACTING (6-8 HOURS)			●	
NASAL, SINUS DECONGESTANT				●

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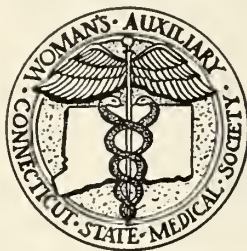
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The Connecticut Nutrition Council, to which the Woman's Auxiliary sends a delegate, will be the topic for this month's column. The Council has been in existence for 21 years, being an "outgrowth of the Connecticut State Nutrition Committee, which had been appointed by the Governor. The objectives of the Council as defined in the constitution are: 'to develop and maintain interest in nutrition as a contributing factor to health, and to promote nutrition in education within the State of Connecticut'. Other objectives are: to assist in the coordination of interest and activities which are concerned with nutrition and health; to be available as an advisory group within the state and to be an aid to seek cooperation and group thinking on programs and needs as developed in the community, state, nation and the world; and to stimulate and encourage workshops and forums on nutrition."

"The Council is organized on a delegate basis so that a member may take information to his agency or organization and in turn bring back information to the Council." Delegates come from various health related organizations of the state, from the home services departments of utility companies, from state agencies, and from food producing industries. The representation is so varied that every phase of the work can be probed and discussed. The Maternal and Child Health Committee is particularly concerned with the diet of expectant mothers and young children; the Connecticut State Dental Association with diet and its relation to tooth decay; the Connecticut State Medical Society, among other things, with quackery in nutrition and false weight reducing diets; the State Department of Education with the teaching of nutrition in the schools and the school lunch program. The educating of students to become home economists and dieticians and their use in the public interest, and the train-

ing of groups such as Girl Scouts and Golden Age groups are also of interest to this Council.

SILVER ANNIVERSARY—MAY 6, 1969

The Constitution of the Woman's Auxiliary lists the objectives of the organization to be:

1. To assist the Connecticut State Medical Society in its program for the advancement of medicine and public health.
2. To coordinate and advise concerning activities of County Auxiliaries.
3. To cultivate friendly relations and promote mutual understanding among physicians' families and with the lay-public.

In honor of 25 years of effort by many women toward these objectives a special program will be held in New Haven on Tuesday, May 6, 1969. An invitation will be received by each member notifying her of the exact time and place. Please keep this date in mind so you may join us for this silver anniversary commemoration.

don't miss the

177th ANNUAL C S M S MEETING

May 13, 14, 15, 1969

Hartford Hilton Hotel, Hartford

—: PLAN NOW TO ATTEND :—

BOOK REVIEWS

TODAY'S HEALTH GUIDE, Revised Edition. A manual of health information and guidance for the American family. Published by the American Medical Association, 537 North Dearborn Street, Chicago, Illinois, 1968. 624 pp. \$5.00.

Reviewed by: LOUIS H. NAHUM

All of us know that the home is the center for healthful living. It is in the home where the homemaker can create an atmosphere, a "climate" in which health will be favored, disease discouraged, life prolonged and above all enriched. This book is intended to help promote the prolongation and enrichment of life.

This health guide is the product of combined knowledge and experience of many doctors and allied scientists. More than 200 people—practicing physicians and specialists, dentists, veterinarians, clergymen, chemists, physicists, nurses, educators, engineers, safety experts, writers, reviewers and members of the AMA headquarters staff have had a role in its preparation.

The guide is a logical outgrowth of the purpose of our profession to serve their patients in every way and this is exactly what it does do. It has full color transparencies of the organs and systems of the human body. It begins with advice of do and don'ts in emergency first aid and ends with calories and sound views about diets. It is a guide for the laymen to sound living practices and a volume of general information about health maintenance and disease prevention not a compendium of home remedies and do-it-yourself medicine.

There are 15 parts covering knowledge of almost every part of health and hygiene that a person can quickly seek and obtain. The AMA has played a vital role in helping to maintain the health of the American people. This book goes a long way to achieve just that. It is a book that should be in every home and every physician owes it to his patients and their families to urge them to have it in their homes. The price of \$5.00 is certainly not enough to pay for the preparation and printing. The difference is the AMA's contribution to the health of the people of this country and the world if they could but learn about it.

THE DARK SIDE OF THE HOUSE. Yale David Koskoff, M.D. and Richard Goldhurst, 209 pages, 2 illustrations, Appendixes, price \$5.95. Dial Press, New York, 1968.

Reviewed by: LOUIS H. NAHUM

There is certainly a correlation between maternal neglect, a hostile environment and a child's hostile behavior and lack of intellectual and emotional development. For now we recognize the crucial nature of childhood. Young children learn whether they have the right example or not. What they learn depends a lot upon the quality of their environment. A mother's approving smile is as surely a learning material as a set of geometric shapes. Millard Wright had neither. He was born to a mother who soon developed cancer and was left an orphan at the age of three. His father was deaf and unmoving and the child grew up with a physical handicap of sight with which he saw the world in skewed images. Unhappiness surrounded his existence that "drilled

and re-drilled him." He was too young to slough off maternal deprivation. He never quite could cope with the love he missed in infancy and childhood. It was an immovable weight upon his psyche.

Repeatedly apprehended for burglary and incarcerated he finally in his fourth offense was ready for life imprisonment. This terrifying prospect led him to an attempted suicide and then commitment to a hospital for the criminally insane. At this point Wright's attorney Louis Little approached Dr. Yale David Koskoff, a celebrated neurosurgeon and neurophysiologist, as to whether he would be willing to perform a frontal lobotomy in hopes of curing Wright's criminal behavior. Little's idea was that as a volunteer for this drastic psychosurgery this patient would be performing a public service that might encourage the Judge to lessen the sentence. With the Court's approval Dr. Koskoff agreed to participate.

Up to then a lobotomy had never been performed on an individual whose brain was not known to be organically damaged or who was not known to be suffering from an acute physical or psychic disorder. These two pioneers then a surgeon and a criminal became enmeshed in social forces unanticipated and beyond their control, those which involved the surgeon on a determined defense of his medical and personal integrity and those which led Wright after being freed into burglarizing and back into prison.

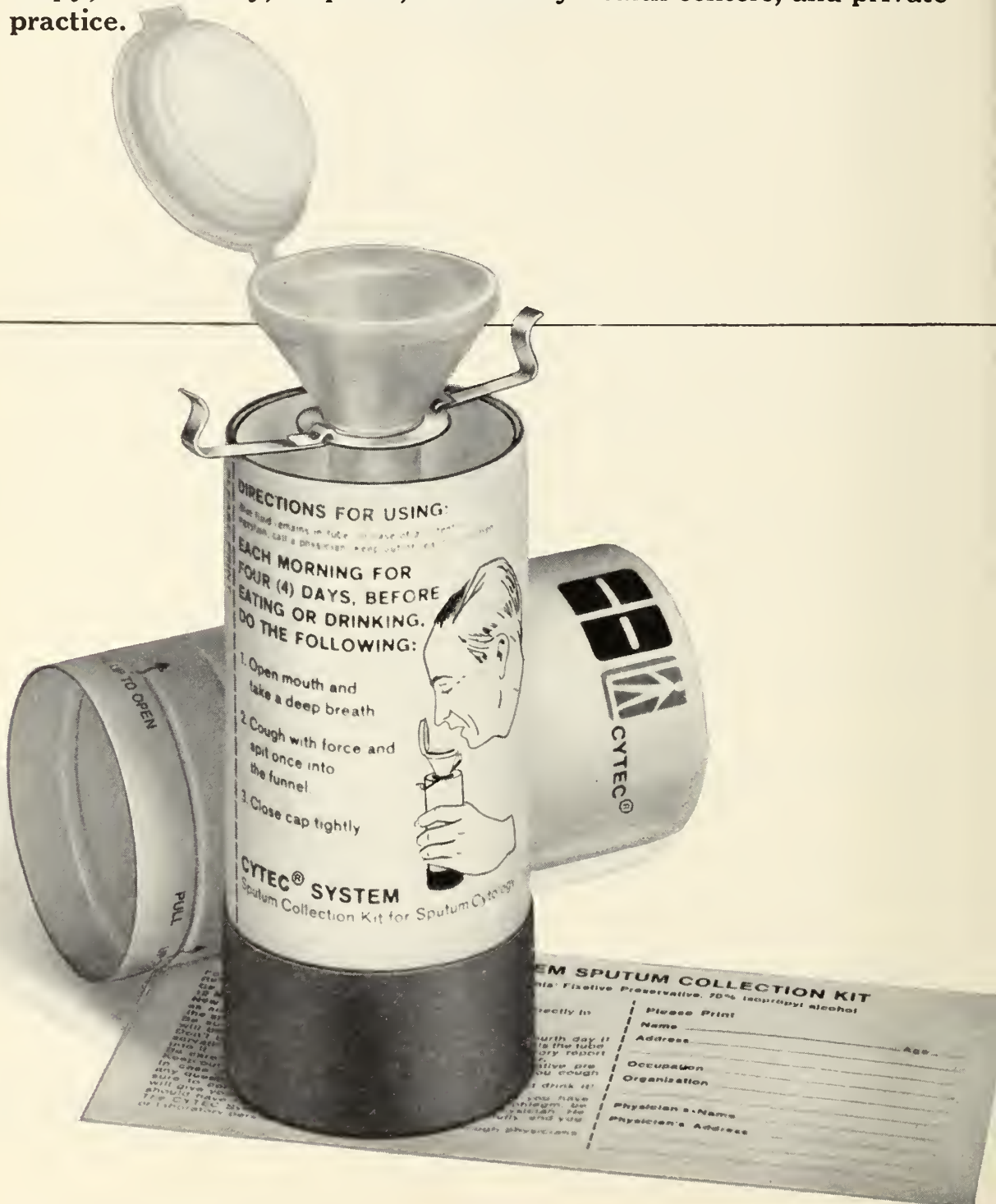
The book is structurally perfect with complete economy of words. In highly dramatic prose Dr. Koskoff and Richard Goldhurst tell for the first time the entire story of Millard from infancy to death. It is a definitive study of the tormented mind of an habitual criminal, the impoverished mental and emotional environment in which he was born, the consequences of abandonment, the punitive nature of our correctional institutions that helped to solidify this man's uncontrollable urge to steal. It is also the most detailed study of the effects of lobotomy ever presented to the American public.

After death by suicide Dr. Koskoff removed the brain—Millard's legacy to science. It appeared in excellent condition. The cuts were where they were intended. There were no surprises. The surface disclosed normal configurations. But there was also a cancer of the stomach with a life expectancy of no more than six months. The brain was entrusted to Dr. Paul Yakovlev of Harvard, a renowned neuropathologist, neurologist, and philosopher. He made a complete study and wrote that Millard's and Koskoff's contribution could not fail to become one of the capital works in surgical psychiatry.

The lesions introduced behavioral changes in awareness, feelings, words and thoughts. A lobotomized man evidently can suffer, can commit suicide. A burglar can go back to his old ways and that restitutive processes in the brain can be organic and partly also psychological. There was no diminution of anxiety following the surgery. Instead Millard showed more distress after lobotomy than before. Apparently awareness of the damage to self elicits greater anxiety. In the last analysis assuming the brain lesions are not overwhelming factors intrinsic in the personality play the decisive role, in short the adaptive capacity of the whole human being remained.

AN IMPORTANT MESSAGE ON SPUTUM CYTOLOGY

Sputum Cytology—practical and economical as a routine diagnostic aid for the detection of lung cancer to be used in conjunction with other diagnostic techniques (such as roentgenology and bronchoscopy) in industry, hospitals, community health centers, and private practice.



AN AID TO THE MEDICAL COMMUNITY: Sputum cytologic screening is an aid in lung cancer detection when used with professional judgment as part of the diagnostic workup of the patient.

Pulmonary exfoliative cytology is a useful diagnostic aid when used in conjunction with other diagnostic techniques in early lung cancer detection; however, problems in sputum collection, difficulties in preparation, and expenses involved have made it impractical for routine screening. As a consequence, it has not been used to the fullest in private, industrial, and public health programs. The CYTEC® System of Sputum Cytology helps overcome most of these problems.

The CYTEC System is sputum cytology with rapidity

Developed by Nuclear Research Associates, Inc., the CYTEC System provides reliable collection, preservation, separation, and concentration of cells as well as automated staining, all with accuracy, uniformity, speed, and simplicity.

This System has been tested for the last few years in industrial and commercial pilot investigation programs as well as in numerous major hospitals.

CYTEC is simple, convenient and easy to use

The CYTEC System provides a sputum collection kit containing a plastic test tube with a built-in funnel which facilitates the collection of early-morning "deep cough" specimens. A tight-fitting cap creates a leak-proof receptacle containing a preservative/fixative which eliminates the need for refrigeration.

The patient simply collects the sputum produced by early-morning "deep coughs," on four separate days, closes the test tube and returns it to his physician, medical director at his place of employment, or public health officer who can then send it in the self-contained mailer directly to our Ca Detection Laboratories for analysis. Reports will be returned only to the designated physician. Photomicrographs showing morphologic cellular changes, if present, accompany the physician's report.

CYTEC can be obtained only through the medical community

CYTEC is being offered *only* to practicing physicians including medical directors of industrial, community, and public health programs. It is being offered as a diagnostic aid to be used in conjunction with other techniques. CYTEC screening results serve as indicators for possible further workup.

A few words about Nuclear Research Associates, Inc., and its Ca Detection Laboratories

Nuclear Research Associates, Inc. is an interdisciplinary organization of physicians, physicists, biologists, chemists, and engineers working in the physical, biological, and medical sciences. The Ca Detection Laboratories represents a portion of Nuclear's recently established biomedical division and is devoted to research and technology in the cancer detection field. CYTEC is the first development to be offered to the medical community by the biomedical division. Others are on their way.

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There then follow a searching analysis of Millard's psychodynamics why he acted out against society, his impulsiveness, shallow feelings, his struggle within himself, the despair. The dynamics of aggression towards self out of a well of despair is clarified by a diagram of the innumerable transactions a person goes through from infancy to death. In essence non-achievement of mature love, the need for punishment was deeply rooted in the man. Lobotomy itself was simply a part suicide in his drift toward death. There is a facsimile of the preoperative and post-operative writing and typing and evidence of a return of this facility to the preoperative level.

Not the least interesting part of the study is Koskoff himself and his involvement with the other character, the patient. The surgeon turns out to be an admirable participant observer, neither sparing himself nor the burglar in the interest of scientific objectivity.

This book will endure as a source book for behavioral scientists, criminologists, sociologists, lawyers and of course the medical profession. But it is more than this, much more—it is something which the public will avidly read for its absorbing tale of a tortured man enmeshed with the law and at the same time an important subject in a fundamental psychosurgical experiment.

ATLAS OF PRECAUTIONARY MEASURES IN GENERAL SURGERY. Edited by *Ivan D. Baronofsky, M.D., Ph.D.* The C. V. Mosby Company, St. Louis, 1968. 281 pp. Illustrated with 111 plates and 132 figures. \$23.50.

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Reviewed by: J. ALFRED FABRO

Dr. Baronofsky is professor and chairman of the Department of Surgery of The Hahnemann Medical School in Philadelphia. With the aid of a fine medical artist, Daisy Stiwell, who sketched the operative illustrations in the operating room, he presents an atlas of those operations performed by him during a period of 6 months.

His preceptor, Doctor Owen H. Wangensteen, states in the preface that Doctor Baronofsky "obviously intends his monograph for the surgeon confronted with the task of orienting himself with reference to certain details of an operation before undertaking it. . . . The combination of a knowledgeable and skillful surgeon and superb illustrations by a talented artist in this effort should ensure a wide audience."

The author himself states that the "purpose of this book is to point out some of the surgical landmarks that, if thought about as one operates, may PREVENT serious complications.

One might rename this book "Defensive Surgery."

Doctor Baronofsky includes most of the common operations, and COMMON must be emphasized, of the gastrointestinal tract encountered by a general surgeon—as done by himself over a period of 6 months. Not included, for example, are surgery for congenital malformations, or gynecological surgery, or vascular problems. The only operation in the neck is thyroidectomy.

On facing pages, one page is devoted to the operation illustrated by the artist, and the opposite page is a step by step, succinct description of it, including a discussion of how to avoid those errors of surgical technique which "make for lack of sleep and many telephone calls during the night for the general surgeon without a resident or staff."

The techniques are only those as done by the author. Only rarely does he describe an alternative or different version of doing a procedure. Except for one, there are no references. Even for an operation which he describes by name, the Ripstein procedure for rectal prolapse, he does not provide the reader with the reference.

I find it difficult to make up my mind to whom Doctor Baronofsky has directed his excellently illustrated Atlas. If it is to the community hospital general surgeon without residents or interns, like the reviewer, I find it lacking in detail for the more serious type of operation. And I hope I don't need a step by step procedure, from the skin incision, for a routine appendectomy.

If it is directed to the trained surgeon, he could have pruned away much of the book in certain aspects and added detail in others—with alternative techniques and references to surgical literature. On the other hand, I should hesitate to let loose in the abdomen a neophyte surgeon or beginning resident with no more than this book.

Doctor Baronofsky himself states that "many excellent texts have outlined the steps of an operation, and many excellent atlases have illustrated the techniques." If authors are going to spend time and effort on such labors of love, they must ask themselves: "Exactly for whom am I writing this?" In spite of its good points, to which Doctor Wangensteen refers in his preface, I find that Doctor Baronofsky has not clearly defined for himself who his reader was to be. I reluctantly conclude that it adds little to the library of the trained surgeon. It can be of help to the surgeon training.



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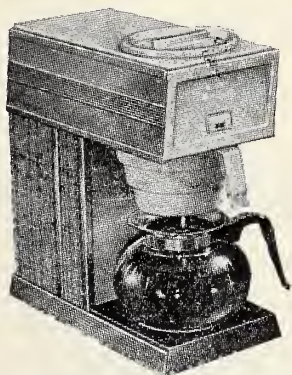
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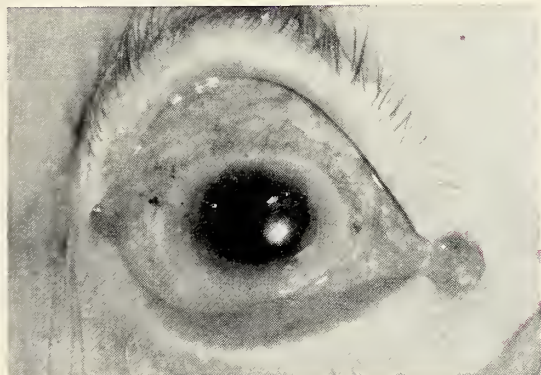


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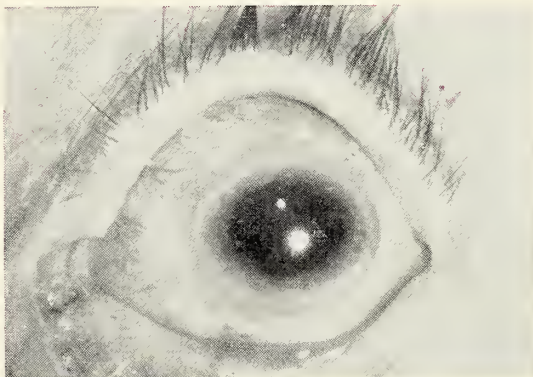
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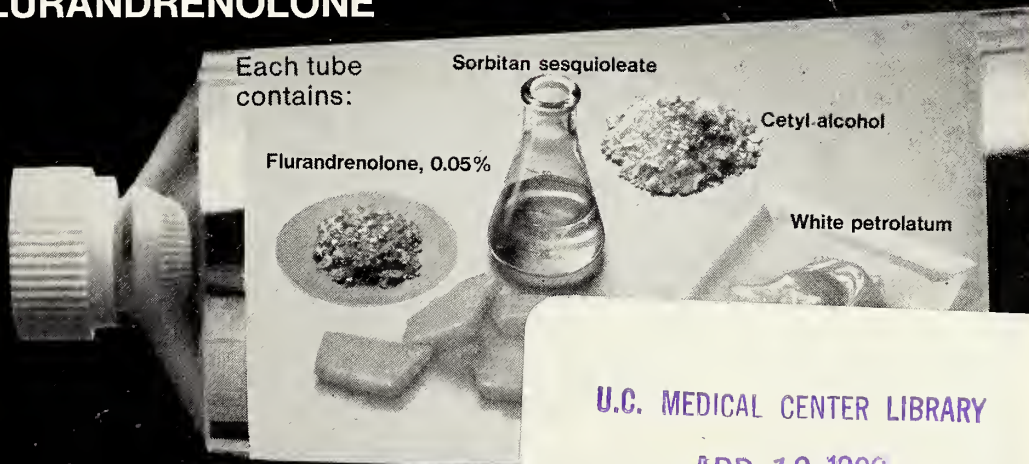
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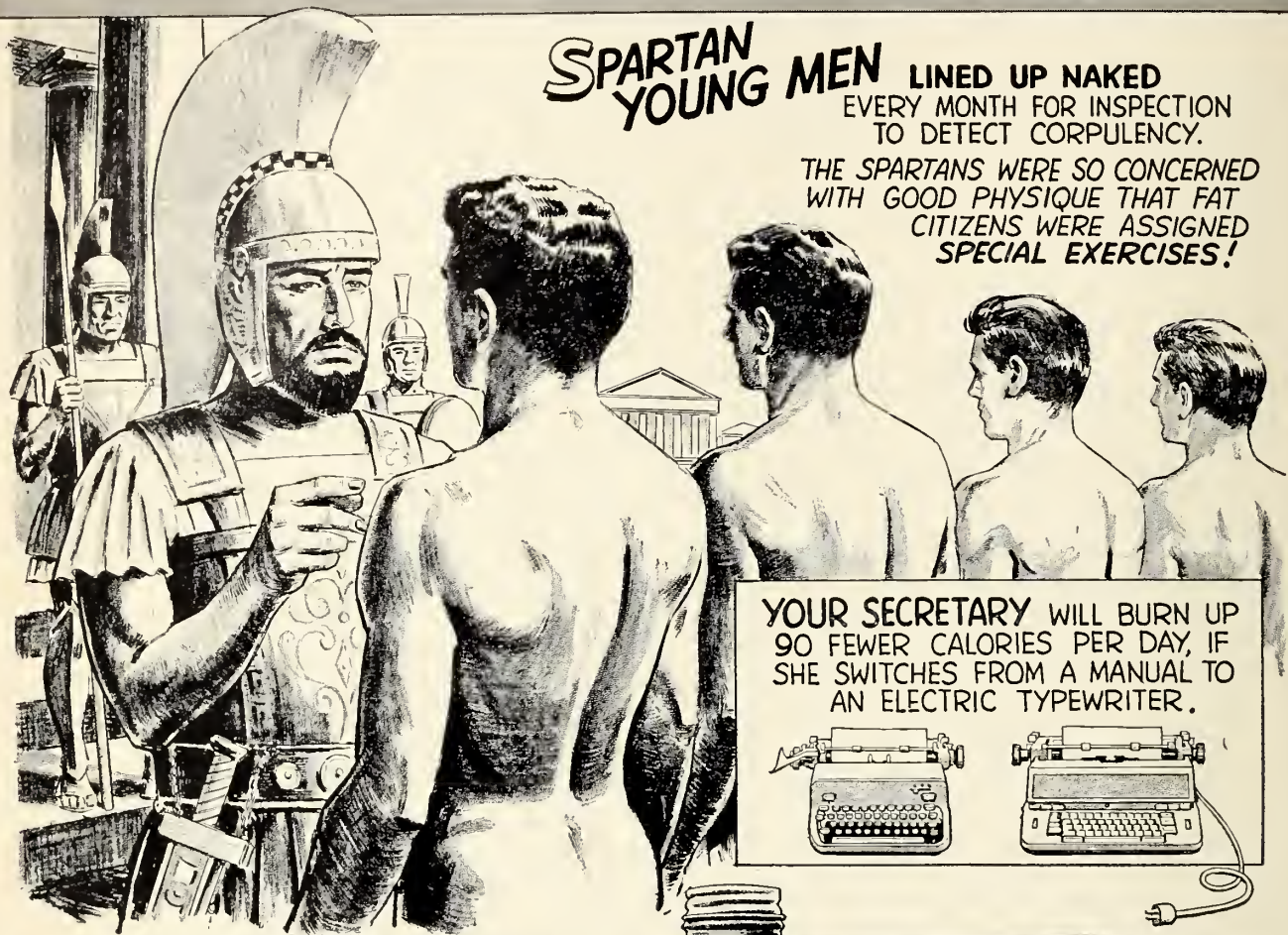
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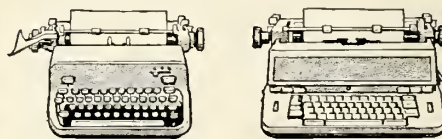
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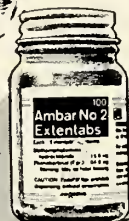
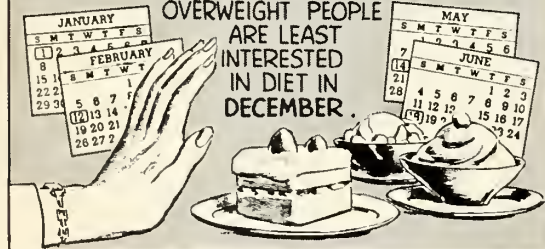


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Connecticut Medicine

editorials

How Do Patients Feel In A Coronary Care Unit

In the recovery room from open-heart surgery sensory monitoring and sleep deprivation were the principle factors in the "new madness of medical progress."¹ What about the equipment of intensive care especially cardiac monitoring devices? What about proximity of other critically ill patients? Hackett et al² found that in general occupants of the coronary care units (CCU) are undercomplainers. The discomforts experienced in the units were more than counterbalanced by the care and personal attention received. In addition the patient is apt to be so preoccupied with his illness that surroundings are hardly noticed particularly because they were well sedated. Then again the patient's welfare is almost entirely dependent on the unit, so that to complain or criticize even when asked to do so is to risk good will of the staff. Generally, however, the unit and its personnel are lavished with praise even as late as six months afterward most of which is deserved.

The monitor came in for intensive study by the psychiatrists. A few patients expressed curiosity about the machine, but none asked specific questions even when they were invited to do so. They accepted what was told them with what seemed to be implicit faith. The majority of patients were either reassured by the monitor or indifferent to its presence. Unless those patients pretended this response or totally repressed fear, their reactions indicate that the machine has an immense potential for giving security, a potential that thus far has been largely overlooked.

If the monitor is introduced by the nurse as a "mechanical guardian angel" expressly designed to keep the heart functioning at maximum efficiency,

the patient instead of dwelling upon its minatory significance, is more inclined to accept the machine as described by the nurse. However, the patient must be prepared for the event of having an accidental alarm in order to be spared this potentially shattering experience. In this way the life saving properties of the monitor can be exploited in a manner most propitious to the patient's emotional well being. In fact sixteen patients actually enjoyed watching the ECG tracings of their neighbors although they had no good reason for it.

Disorientation in time occurred in less than half of the patients sampled. It was mild, occasioned no trouble to the patient and was easily corrected by nurses or relatives. Delirium was lower in this study than in that of Parker and Hodge.³ There were of course no post-cardiotomy patients. Also the patients were perhaps under-medicated for pain, apprehensiveness and sleep. The idea was that narcotics, sedatives and tranquilizers might enhance disorientation and confusion. The authors also found a paucity of dreaming including nightmares which was taken to be due to sparse amount of sedatives and sleeping medication given them. In spite of this it is remarkable that so few major psychiatric complications arose in a setting that provided sleep deprivation, violent fluctuations in sensory input ranging from monotony to sudden terror and always the constant threat of death.

It is not surprising that many patients were anxious and depressed and yet showed little evidence of serious panic reactions and major depressions. The defense of denial was very actively employed and this may account for the mildness of the affective response. We cannot know whether the patients were merely pretending to be calm. This is why when possible one should consider using anti-depressant agents particularly those that have a

ABOUT THE COVER

A new technique of cataract removal under investigation by Dr. Charles D. Kelman at Manhattan Eye, Ear and Throat Hospital, uses an incision one-tenth the size of the usual one, and is making possible results similar to that of the sixty year old patient shown above. Hospitalization time was reduced to three days and visual results in both eyes are identical. See *February issue, page 77.* (photos courtesy of Dr. Kelman, *JAMA*, Nov. 25, 1968.)

sedative action the first few days before the antidepressant effect emerges.⁴ Perhaps this is the reason that most patients were glad to leave the unit when the time came. Transfer out of the unit was in addition tangible proof of their improvement, although a few missed the instant attention given their needs by the nurses and four of the forty-five actually feared to leave.

It is possible also that drugs such as amitryptiline would lessen the persistent anxiety in patients after cardiac arrest had been overcome and the violent nightmares associated with this event as reported by Druss and Kornfeld.⁵ Hackett's experience, however, in a smaller number of patients, though similar, also incriminated sleeping pills and idleness which when corrected led to an abrupt cessation of these responses.

What is the response of the patients who witness the shattering experience of cardiac arrest in another patient? Hackett found that much depends upon the staff as well as the patients' psychological defenses. If death occurred, the staff quickly reassured the survivor that the deceased's heart was much worse than his. No matter how obvious the excuse, the patients seemed to accept this without question or reservation. Patients seem able to grasp the most comforting meaning from a serious event while denying the most threatening. Even when the patient with arrest was of the same age as the patient onlooker some reason was always found to differentiate the onlooker's condition from that of the victim. The tendency was to extract from the situation only the elements that could bolster denial and thus restrain fear.

One of course must question whether these responses actually represent the true feelings. There is evidence that witnessing an arrest may cause the observer to ask for a private room in subsequent admissions for coronary care. But we do not really have enough evidence to answer this question. Like the patients described by Druss and Kornfeld, those of this series that experienced cardiac arrest could not recall much of the event. Largely because of the total amnesia of the arrest, none of the six could assimilate it as part of the hospital experience. Two who spoke of having died and returned made only little of it. The impression remained that unless constantly reminded they would forget that their heart had required assistance to regain its beat.

The use of denial as a defense against fear and anxiety is well known as an important mechanism and has been dealt with at length in the psychiatric

literature. It is perhaps the most commonly used mental mechanism to cope with acute emotional stress. The reason for identifying the various types of denial has to do with their management and perhaps their prognosis as well. The patient with only partial denial wants reassurance but does not know how to ask for it directly. These may actually be more apprehensive than they appear and might benefit from sedation. Reassurance, encouragement and even heavy sedation might also be the treatment of choice for the minimal denier.

It is difficult to offer a method of approach for the major denier because we know less about him than about the minimal and partial denier. However, the ability to deny may have value for immediate survival. Man seems to have a faculty for defending himself against emotional stress in endlessly inventive ways not the least of which is denial. We know so little about how a man manages to deny obvious stress and even less about whether this ability to deny can protect his cardiovascular system against sympathetic nervous system effects upon the heart particularly. We do know, however, that nor-epinephrine release in the heart and adrenaline release by the adrenals can precipitate arrhythmias and place an undue burden on a damaged heart. Perhaps this is why the sleep treatment of the acute phase of myocardial infarction has shown such gratifying results.⁴

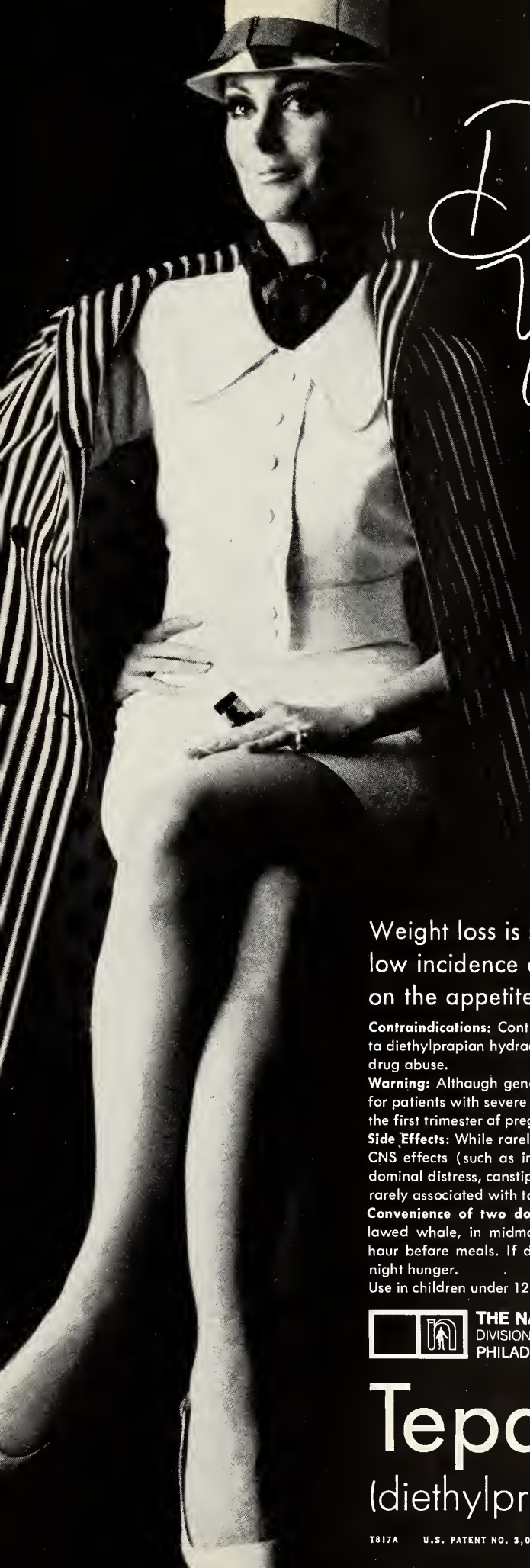
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References

1. Nahum, L. H.: Madness in the recovery room from open-heart surgery or "they kept waking me up." *Conn. Med.*, 29: 771, 1965.
2. Hackett, T. P., Cassem, N. H. and Wishnic, H. A.: The coronary care unit. *New Eng. J. Med.*, 279: 1365, December 19, 1968.
3. Parker, D. L. and Hodge, J. R.: Delirium in coronary care unit. *JAMA*, 21: 702, 1967.
4. Nahum, L. H.: Sleep treatment in acute myocardial infarction. *Conn. Med.*, 32: 642, September 1968.
5. Druss, R. G. and Kornfeld, D. S.: Survivors of cardiac arrest psychiatric study. *JAMA*, 201: 291, 1967.

Approach To Medical Education At Vancouver

Primary health care is that which takes place in the home and doctor's office. It is generally recognized now that it will not be possible to educate enough physicians willing to engage in this type of practice especially considering the growing needs of an increasing population at the same time that the doctor has so much more to offer as knowledge



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in health science increases with great rapidity. One challenge of primary health care then, is to provide the physician with sufficient assistance since he is unable any longer to do it all himself. In the hospital we have mobilized many other health professions to assist the physician, nurse, dietitian, physical therapist, pharmacist, clinical psychologist, social worker all assisting the physician and extending his influence. As a result when a patient is in the hospital the physician can provide health services with efficiency, economy of effort, and time. This is not possible in the physician's office or patient's home so that we find the physician providing health services in a manner virtually unchanged in the past twenty-five years.

One of the major requirements for the future then, is to expand the influence of the diminishing number of primary care physicians. A plan is obviously necessary to train assistants to the physician in the provision of primary health care. It must involve training the same kind of personnel for assistance to physicians in the community as he has to assist him so well in the hospital. At University of British Columbia in Vancouver¹ they decided to integrate the teaching of existing health professions in such a way that they might better understand and appreciate what each professional group could contribute. If they could create a more meaningful role for the allied health professions perhaps they could attract more people to them. This would obviate the need for a new and special type assistant like the medical corpsman in the army. The great difficulty encountered in Vancouver was the lack of a model to assist them in the development of interprofessional education in the health sciences. No such scheme was in operation anywhere to guide them and they had to fashion one from scratch.

They set to work on a design of a health training facility in which would be registered some 2,200 students. All the teaching of medical, dental, nursing, pharmacist and students in rehabilitation medicine is to take place in this complex. A very significant amount of the teaching of students in dietetics, social work and clinical psychology is also to be carried out in this setting. The stupendous problems such as teaching space, instructional resources, design of buildings to permit joint teaching of all the health professions was simple compared to problems involved in solution of the methods by means of which this interprofessional education could be carried out.

After a while there emerged a body of knowledge primarily related to community health methods of evaluation of health services required by a community and how to bring them into operation. Such knowledge equally important to the social worker for example as it was to the physician. They found that the teaching of this material could well be undertaken in very large groups comprising students from all of the health professions by appropriate teachers from any one of the facilities concerned. The problem of exposing all students in the health profession to teaching in the pre-clinical sciences was undertaken by employing three levels of courses offered in the basic science department.

One level was very detailed and made suitable for medical and dental students. A second level was made suitable to second and third year students in the faculty of sciences as well as nurses, rehabilitation therapists and others. The third level consisted of survey courses permitting dietitians and others to learn something of the philosophy and the vocabulary of the basic medical sciences departments upon which clinical medicine is based. Another approach was in the area of combined clinical training begun on classes in psychiatry for second year medical students, students in rehabilitation medicine and nursing students as well. To lead and organize this complicated integrative teaching program they chose a young physician who had been in practice for ten years, who was aware of the problems inherent in this activity, who introduced the present curriculum.

A course in the first year of medicine brings medical students into contact with relatively normal families and they made home visits at regular intervals during the year. They learned interviewing techniques, growth and development and other aspects of medicine which gradually permitted them to serve increasingly as the family's health advisor during the year. Nursing students now make visits together with medical students who then presented problems of the family to the remainder of the class. A survey type of course in the department of pathology is offered to third year students in nursing and is audited by home economic students and students of pharmacy. The pharmacy students now enter homes with Medical students and the other disciplines each attempting to bring his particular background to the problems uncovered.

An interesting experiment is one in which architecture students involved in urban planning to-

gether with second year medical students are jointly bringing the health problems of urban planning to the fore. In addition a strong department of the history of health sciences offers courses to first year students of each faculty and school in the health sciences, an introductory course of approximately six weeks. This is then picked up by each separate school and develop their own specific historical material for further more extensive examination.

The most important shared educational opportunity will probably come in a family practice unit under the direction of the various faculties. The unit will care for 600 families. It is being organized by a physician who has completed his training in internal medicine and psychiatry and who has demonstrated for many years a keen interest in the provision of a continuity of care. Three general practitioners carry the major part of the practice, and they are joined by nurses, pharmacists, social workers, clinical psychologists and others. Students of all health professions will participate in the services which are provided in the patient's home and in the clinic offices twenty-four hours a day and seven days a week. McCreary reports that the students themselves have forged far ahead of the faculty in enthusiasm for this type of interprofessional teaching and are anxious to press on with further integration.

A definite pattern is beginning to emerge toward the goal of integrating professional teaching. Each of the professional groups in the health sciences are profiting at the beginning of their period of instruction from a thoroughly intensive experience lasting about three months in which they jointly make home and institutional visits, observe the work of health professionals and focus their attention upon the interaction between the patient and the professional who is trying to serve him. They explore living conditions and the social and health problems in urban and rural communities. On returning they take part in discussions and are directed toward recommended material in the relevant fields of sociology, anthropology, epidemiology, statistics and biology. The planners of curriculum hope that as a result of this exercise each student would realize early in his professional education that they are all engaged in solving problems of health.

The second stage in the education of all health professionals is a core curriculum which will vary in duration for the different groups. The medical students will require two years. The nursing and others would require much less time with relative-

ly separate pursuits and little integration. The third stage in the education of the health professionals would be of shorter duration, a period in which experiences in depth in elected areas and to the students own particular discipline. The final phase in the education of all groups is experience in practice in which all interact together as they did at the initial exposure at the beginning of the professional training and as they function later in a hospital.

There are bound to be difficulties in seeing this new approach to medical education become successful. One great advantage at Vancouver is that it is starting from scratch and can ensure that appointments of senior people to the faculty are made to individuals who find the program attractive and are prepared to give it their support.

Whether the experiment succeeds or fails, it is a response to a new era in medical practice in which the practice of medicine is recognized as a social activity with the need of extending medical care to the whole community.

L.H.N.

Reference

1. McCreary, J. F.: The health team approach to medical education. *JAMA*, 206: 1554, November 11, 1968.

RNA Induced Interferon In Viral Infections Of The Eye

By inducing interferon production in rabbit's eyes, Park and Baron have effectively treated severely established keratoconjunctivitis as late as three days after infection. They introduced herpes simplex virus into the eyes of anesthetized rabbits after the cornea had been scratched. They then began treatment with an interferon inducer termed PI:C. This is a synthetic double stranded RNA copolymer found with polyinosinic acid and cytidilic acid. The rabbits were divided into groups of two and treatment of the first pair began three hours after herpes simplex virus inoculation. Each eye received 0.1 ml. of PI:C three times daily and the treatment continued for six days. In other rabbit pairs treatment was begun one to four days after inoculation.

Only minimal keratoconjunctivitis developed in those rabbits first treated three hours to twenty-four hours after virus inoculation. Moderate to severe conjunctivitis developed in rabbits whose treatment did not begin until the second or third day after inoculation. However, the moderately severe conjunctivitis began to clear after four to

five days of treatment with PI:C. By the thirteenth day there was almost complete healing. No therapeutic effect was noted in rabbits in which treatment was delayed until the fourth day after inoculation. These rabbits and all of the control group animals developed severe keratoconjunctivitis and about one-third died.

Earlier investigations showed that induced interferon production followed the use of several substances, but RNA has very limited toxicity and interferon levels in Park and Baron's animals were usually high. On days one and two of treatment interferon levels were 13,000 international units/ml. of serum. The untreated animals produced no interferon.

It has been known for some time that applying interferon prevents a wide range of viral infections.¹ Until recently, however, it was impossible to obtain enough of the substance to treat already established disease. The success of RNA as an inducer of interferon to combat herpes simplex virus infections of the eye, successfully, should encourage its use to be extended to other virus infections. Since there are many viruses that are more sensitive than herpes simplex to the antiviral effect of interferon, we may expect that this method of interferon production will be effective therapy of these infections also. Surely if inducers of interferon in rabbit eye infections are so successful it seems reasonable that RNA induced interferon will find application in viral infections of the human eye also.

L.H.N.

Reference

1. Park, J. A. and Baron, S.: Synthetic RNA stimulates interferon in eye infections caused by herpes simplex virus. *JAMA*, 206: 2223, December 2, 1968.

The Problems Of The Volunteers In Medical Research

The search for new drugs and new techniques of medical care requires that man be the final experimental animal. The safeguards for volunteers have thus far assumed two forms. The first has been formal review. Committees in institutions and governmental agencies often review the purposes, methods, risks and precautions in experiments involving human volunteers. The second form long established though sometimes neglected has been the safeguard of informed consent. This procedure requires that before the volunteer consents to the experiment he be given a clear explanation of the risks and discomforts he might

expect during the experiment. The question is that as new technical procedures continue to be developed and as more extreme experimental situations present themselves, will the standard forms of review and informed consent remain adequate safeguards for the welfare of the human subject.

Martin et al¹ report the results of three studies of the problem of the volunteer in medical research. In the first, prisoners who had been asked to participate in a malaria experiment were interviewed to determine why they had or had not volunteered and the extent to which they truly understood the risks they might face in the course of the experiment. The physician carefully explained the malaria project to the inmates at the Jackson County jail in Kansas City. They were told of the need for human subjects and the probable risks involved. He was to be paid for participation in money but not a reduction of sentence.

Those who did volunteer were told in detail the process of the disease, and the discomfort they would experience. Behavioral scientists who were not involved in the project studied two groups. Those who did volunteer were ill with malaria and successfully recovered. The second group consisted of those who could have volunteered but didn't. The inmates who volunteered understood no better or worse the nature of the disease and its threat to human life than those who did not volunteer. This was in spite of the fact that they signed the "informed consent" document and continued to receive detailed information throughout the program. In spite of explanations, the volunteers continued to describe the project in terms of "high risk."

The results of the study indicate that the act of volunteering does not result from a logical process resulting from an understanding of the information provided and a consideration of the alternatives open to him. The volunteer's comprehension of "risk" is little different from that of nonvolunteers and where it does vary it is certainly not more accurate. More remarkable was the fact that very few in either group cited "risk" as a consideration in their decision. It became apparent that there were other issues involved in the decision of the volunteer. One was altruism and the other was money. Both groups uniformly expressed belief in the importance of clinical research as a means of discovering new and better "cures" for disease.

Nearly all the nonvolunteers believed that volunteering for such an enterprise was an "act of courage." They gave a wide variety of personal rea-

sons for not volunteering and at the same time stated or implied respect for those who did volunteer. The almost universal respect among nonparticipants for those who did volunteer may thus offer some clue to the other group's reasons for volunteering. Society at large has the mistaken notion that because life has a low status and few privileges that therefore a system of privileges does not operate within the prison itself. The opportunity in prison to assert one's superiority are few and those that do exist are open to only a limited number of inmates. But participating in the malaria experiment provided many with a real chance to demonstrate their importance not only to the other inmates but to the jailers themselves and it is quite possible that this consideration takes precedence over the weighing of risks and benefits implied by the informed consent procedure.

What then does informed consent really represent? The decision to volunteer involves far more than the simple transfer of accurate information about the risks a subject may face in a clinical experiment followed by the so-called "free exercise" of individual will. The signed document does indeed represent the volunteers consent. However the act of consenting is not real evidence of informed understanding. Influences of environment and peer group seem to have more bearing on the decision to volunteer than explanations of the experiment itself. The decision to participate is made within a social context. Human beings adapt and operate on values and attitudes of the group in which they hold membership. In fact continued membership, status prestige, esteem depends on how well the person continues to fulfill the precepts and expectations of the group.

These statements apply not only to groups of prisoners but the Martin group found them equally applicable to ministers, doctors, janitors, salesmen, nurses, machinists as well. They apply to the affluent and the poor, to the influential and the common man alike. The decision to volunteer or to refuse to participate in medical research is assuredly affected by the above considerations. It appears that a strong sense of altruism is not altogether dead in the modern world. Respondents in the group on personal willingness and opinions about volunteerism particularly in the nonprofessional group believed that "human responsibility" includes an obligation to help improve the "state of living" contingent to some degree upon family responsibilities.

Voluntary participation received strong endorsement from all interviewed. Since it is from the general public that future subjects for clinical research must come, it would appear mandatory that the discussion of human participation in medical research be taken to the public. In conceptualizing and designing experiments one should be careful to make certain that the decisions on the use of human subjects reflect the sentiments of the total community for somewhere in its evolution the "new" medical ethic must be reconciled with the views of the public.

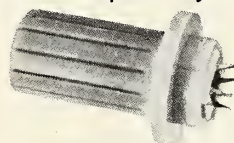
L.H.N.

Reference

1. Martin, D. C., Arnold, J. D., Zimmerman, T. F. and Richart, R. H.: Human subjects in clinical research—a report of three studies. *New Eng. J. Med.*, 279: 1426, December 26, 1968.

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Origin Of Cancer: I. Evolution Of Mitotic Control

A unicellular organism moves away from its sister after division. Multicellular organisms remain together. This means an increased mutual adhesion between the cells and this requires a mechanism for limiting reproduction of the individual cells, a mechanism for the control of cell division if the organism is not to destroy itself by uninhibited growth. There would have to be an evolutionary change, one that could give rise to a multicelled organism and a mechanism for mitotic control built in. In the multicelled organism, cells adhere to each other. We should therefore look carefully at cell adhesion to see if it can offer a basis for regulating mitosis in the multicelled animals.

In higher animals the rate of cell division is closely related to the pattern of cell growth. What can be the mechanism which controls both movement and arrangement of cells as well as their rate of reproduction. Carter¹ suggests mutual adhesion between cells as the mechanism. We have long recognized a significant relationship between cell movement and adhesion. For example cells in culture will move up a gradient of increasing relative adhesiveness with greatly enhanced efficiency and in a highly directional manner. This phenomenon (haptotaxis) appears to represent a fundamental principle of cell movement. This kind of movement depends on adhesive forces between cell and substrate. Movement of cells in a direction demands therefore an imbalance of adhesive forces in the cell periphery. This imbalance is provided in part by the substrate itself.

If tissue cells have no motile capacity then they must be moved in accordance with the local surface forces to which they are subjected. In wound healing there is simultaneous cell division and cell migration. In embryogenesis continually changing cell to cell relationships are correlated with a high motile rate. In cancer a tendency to enhanced mitotic activity is accompanied by excessive cell movement, the peripheral aspects of which are manifested as invasion. Normal adult tissues with a high mitotic rate usually show a correspondingly high rate of cell loss, necessitating continuous rearrangement of the remaining cells. Analogous situations exist in vitro cell culture and show a similar correlation between cell movement and cell division.

If cell movement is an essentially "passive" phenomenon caused by an imbalance of adhesive

forces at the cell periphery, it should cease completely when this imbalance is resolved. This will occur when the cell surface as a whole approaches a stable equilibrium with respect to its local environment. Cell surface stability therefore can only be acquired when an appropriate mutual arrangement has been established between neighboring cells. The actual arrangement achieved will then be dependent on the differing surface properties of the cells and non-cellular elements involved and will thus correspond to the normal architecture of the tissues.

This would mean that cell movement and cell surface architecture are considered to be regulated through precisely the same mechanism and must not be treated separately. There are specialized regions of cell contact such as desmosomes and tight junctions but these could serve in a secondary capacity to reinforce the structural integrity of a particular cell arrangement. Such specialized regions however generally do not develop between cells which are moving in relation to each other. In consequence their formation is probably dependent on the previous attainment of a thermodynamic equilibrium with respect to the cell surfaces.

If the regulation of mitosis can now be related to the concept of cell surface stability, which in practice means the stability of the cell membrane, perhaps here is the fundamental link which integrates the rate of cell division with the pattern of cell growth. Any cell membrane would be considered unstable if its physical relationship with other cells was constantly changing. When the membrane changes its form as in pinocytosis, it must be regarded as an indication of physical instability. Whatever the mechanism of pinocytosis, it is clear that the cell membrane must be free to change and invaginate. If a cell is surrounded by other cells in apposition, obviously it must break contact with these cells at least over a limited area before pinocytosis can occur. Any factor which tends to upset a stable adhesive relationship between the cell surface and surrounding structures may therefore be regarded as potentially conducive to pinocytosis.

Carter's thesis, therefore, is that mitotic homeostasis is primarily controlled by the degree of physical stability of the cell membrane. The question therefore is how far does this proposition satisfy the theoretical requirements for a basic mechanism of growth control. If the primary mechanism is dependent on mutual cell adhesion, it satisfies one

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of the requirements of a basic mechanism. The cell adhesion mechanism satisfies the criterion that it can function in a primitive community of identical cells. This mechanism also makes the essential link between growth rate and growth pattern. The mechanism could explain adaptability and evolutionary refinements. The stability of the cell membrane can of course be affected by physical as well as chemical factors. Loss of cells from a previously stable arrangement would for example create a temporary instability which could be satisfied only when these have been replaced.

On the gross scale the physical forces exerted by one tissue or organ on another would be an important factor in allowing them to accommodate to each other. For example the physical stretching of skin over a growing limb could alter the mutual relationships of individual cells and create instability which would increase the mitotic rate of cells in the skin and allow it to keep in step with the growth of the limb as a whole. Several hormones such as growth hormone, gonadal hormones are known to be concerned with growth control. They might alter the synthetic biochemistry of specific cells to change their surface chemistry or perhaps they alter surface properties of target cells by specific adsorption of hormones to the cell surface.

There thus appears to be a fundamental inter-relationship of cell adhesion, cell movement, cell arrangement and cell division. In cell adhesion we may find not only the basis for the mechanism of differentiation, but also a means of relating it to the other main aspects of cell interaction, one of which is cancer.

L.H.N.

Reference

1. Carter, S. B.: Tissue homeostasis and the biological basis of cancer. *Nature*, 220: 970, December 7, 1968.

Another Endocrine Gland—The Thymus

There are several postulates that must be satisfied to establish that a given organ is an endocrine organ. One is to ablate the organ and then find specific physiological or biochemical alterations and deficiencies. The evidence in support of this postulate is clear. Thymectomy does indeed result in definite deficiencies. The early work needs to be disregarded because of poor operative techniques, lack of knowledge of species variation and ages of animals used. Thymectomy is difficult in adult animals and the state of lymphoid development at

birth varies from species to species. Nevertheless, it is interesting that Restelle in 1845 operated upon 98 sheep, dogs and calves, all of whom died from 9-23 days after the operation because of infection.

At the present time it is clearly established that removal of thymus is followed by deleterious consequences to the operated animal with the severity of the results related to the age at which thymectomy is performed. In neonatal mice and rabbits thymectomy prevents the development of immunological competence,¹ retards growth, leads to wasting and a marked diminution in the lymphocyte population.² The deficiency in lymphocytes is more striking the younger the age at which thymectomy is performed and is reflected in the number of circulating lymphocytes and in the total population of lymphocytes present in the lymphoid organs. Furthermore a thymectomized animal will not restore his lymphocyte population if he is first irradiated. Such observations all point to the conclusion that the circulating lymphocyte as well as the lymphoid organs in which they have their origin are dependent for their development upon a normally functioning thymus gland.

The role of the thymus in the development of immunobiological competence appears to be correlated with the role of lymphoid tissue in antibody production. Normal lymphocytes contain gammaglobulin and these lymphocytes from immunized animals contain antibodies. Such lymphocytes are also capable of passive immunity transfer.

There are many clinical and experimental studies often involving thymectomy which exhibit a definite relationship between the thymus and the etiology of a variety of disorders ranging from those considered to have an auto-immune etiologic component, myasthenia gravis, lupus erythematosus, rheumatoid arthritis, polymyositis, all the way to neoplastic disorders such as lymphoid leukemia, polyoma tumor induction and skin cancer. For example there is an increase in the remission rate in patients with myasthenia gravis following thymectomy. There is a decrease in the incidence of lymphatic leukemia in a high incidence strain of mouse after thymectomy.³ There is shortening of tumor development by chemical carcinogen or tumor viruses after removal of the thymus.

It is thus possible to draw several implications from such findings. The most important is the correlation between immunobiological deficiencies with accompanying thymic dysfunction and patholog-

ical disease states. It appears that the antibody synthesizing mechanisms controlled by the thymus have hitherto unsuspected importance in the onset and progression of many types of diseases. Whether the ultimate control of these processes is determined by seeding of thymic cells to the periphery or secretion of thymic humoral factors or both has not been established definitely. However enough information is available to suggest a positive role for thymic humoral factors. Since thymectomy does result in specific physiological and biochemical alterations and deficiencies, this gives strong support to the first postulate for establishing an organ as an endocrine gland.

The second postulate holds that replacement of the extirpated organ by transplantation or administration of a suitable extract from the removed tissue should restore the disturbed physiology to normal. White and his co-workers⁴ have prepared a thymic extract, thymosin which appears to influence not only immunologic parameters and lymphoid tissue size and function but also glucose metabolism, ATP synthesis, fertility, calcium deposition. It is quite likely that the thymus as is the case for the hypophysis and adrenal gland may secrete more than one hormone and thus influence several of the hormonal functions of the body. This extract can lead to partial or complete replacement of specific functions of the extirpated thymus. Skin color in frogs lost by thymectomy can be restored by thymic extract. Normal growth and immunobiological phenomena can be restored by thymic grafts into thymectomized animals. White's thymosin increases the number of circulating and tissue lymphocytes. Most striking has been marked stimulation of lymphoid tissue regeneration observed as a result of injection of thymosin in mice previously exposed to whole body irradiation. Thus partial or complete replacement of specific functions of the extirpated thymus can be achieved by the administration of suitable extracts of this tissue.

Postulate three holds that large amounts of an extract of the gland to normal animals should result in an exaggerated supply of the hormonal product and exaggerated response. This has been achieved by White et al, who administered large amounts of thymosin daily to guinea pigs and mice and produced a hypertrophy of lymphoid tissue exhibited by increased weight and increased mitotic activity in lymphocytes in lymph nodes.

Postulate four requires isolation in pure form and characterization of the active hormonal principles as they occur in the gland and blood. White

et al, have already achieved further purification and characterization of thymosin and also another hormone thymostatin which inhibits the action of thymosin.

This examination of the growth of our knowledge about the thymus brings to light much new data that gives an affirmative answer to the question whether the thymus is an endocrine gland. It may be anticipated on the basis of existing knowledge that the endocrine role of the thymus will prove to be a fertile field for investigation and that the results will have significance in a number of areas of experimental and human biology such as histocompatibility immunity to infection, and even cancer.

L.H.N.

References

1. Nahum, L. H.: The Thymus: 3. Immune Tolerance And Autoimmunity. *Conn. Med.*, 29: 552, August 1965.
2. Nahum, L. H.: The Thymus: 1. Its Role In Lymphocyte Production. *Conn. Med.*, 28: 791, November 1964.
3. Nahum, L. H.: The role of the thymus in experimental leukemia. *Conn. Med.*, 26: 495, August 1962.
4. White, A. and Goldstein, H. L.: Is the thymus an endocrine gland? Old problem new data. *Perspectives in Biology and Medicine*, 11: 475, 1968.



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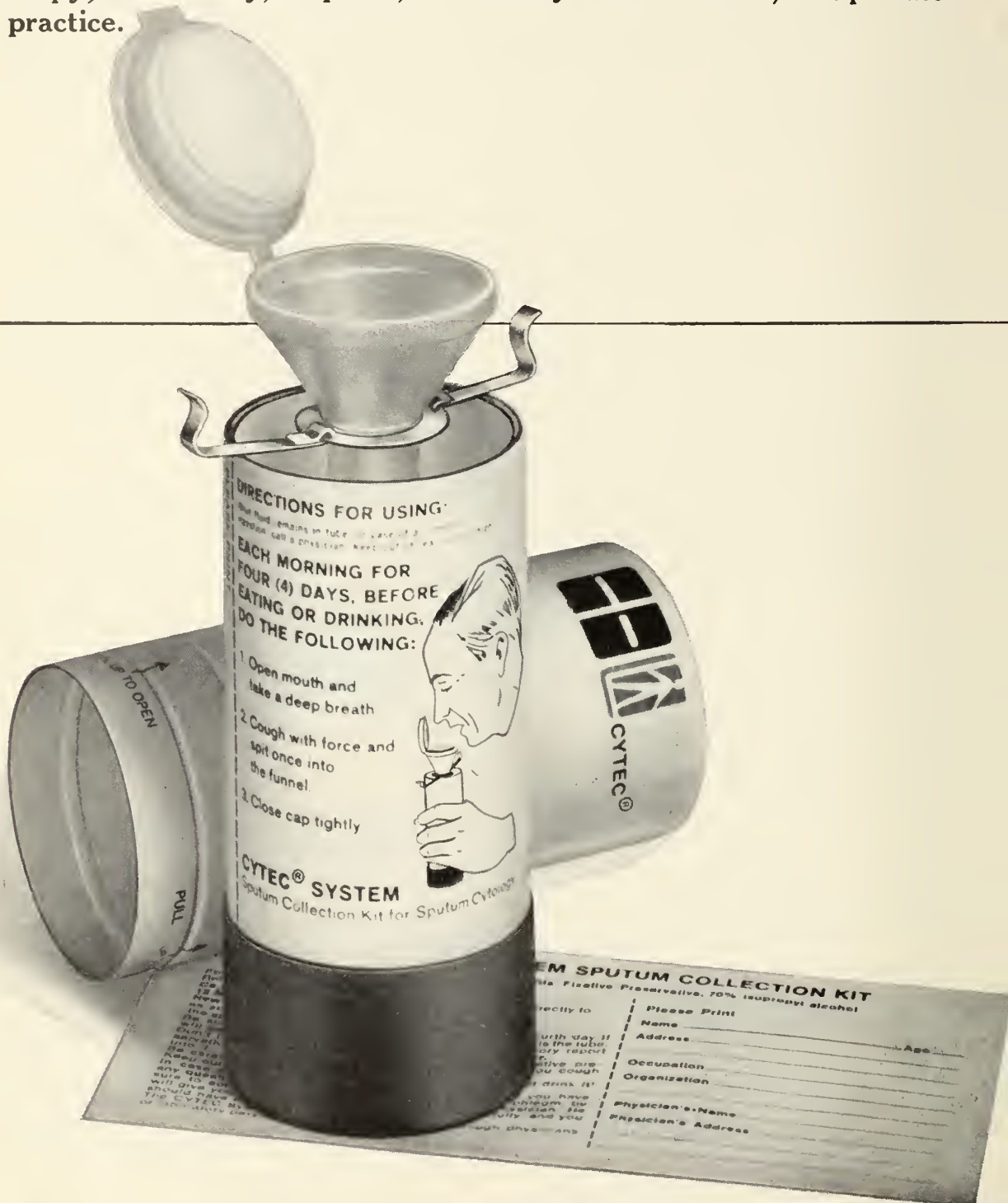
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Fluoride In Otosclerosis

Schambaugh¹ points out that the term otosclerosis is a misnomer. It is in reality a localized osteoporosis of the labyrinthine capsule. It was at first applied to ankylosis of the stapes at a time when the fixation was believed to be secondary to sclerotic changes in the mucus membrane of the lymphatic cavity. Now we know that the fixation is due to a primary bone disease of the labyrinthine capsule. As a bone disease it takes its place with osteoporosis and osteitis deformans (Paget's disease).

The frequency of the osteosclerotic bone lesion as demonstrated by sectioning of the temporal bone at autopsy was established by Guild.² In 1161 routine autopsies he found a focus of otosclerosis under age five in less than 0.6 per cent, but an increasing incidence with age so that at age fifty it is found in 10 per cent of males and in 18.5 per cent of white females. Its incidence is very low in the blacks occurring in about only 1 per cent.

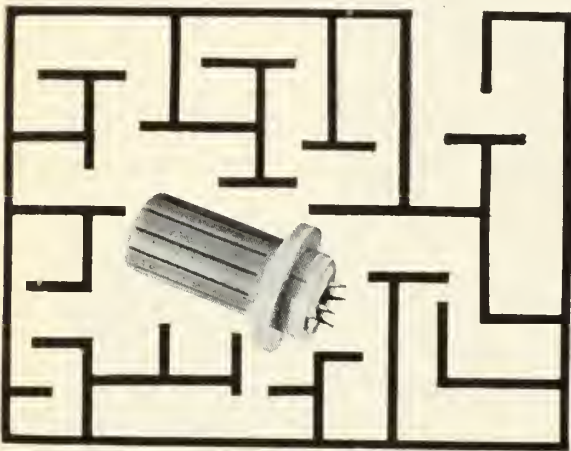
Generally the pathologic process remains quite small without producing clinical symptoms. Only in 12 per cent of ears with otosclerosis did the focus reach the oval window and foot plate of the stapes, producing a conductive hearing loss. These are termed stapedial otosclerosis and constitute the

most frequent cause of progressive conductive type of hearing loss in adult life. In the majority of cases of otosclerotic fixation of the stapes there is also involvement of the wall of the cochlea with a sensory-neural type of hearing loss as well. It was with the hope of finding a way to promote recalcification and inactivation of an actively growing otosclerotic focus so as to retard or arrest the progressive sensory neural loss of cochlear otosclerosis that Schambaugh undertook a series of experiments of fluoride and bone disorders in general.

The etiology of the otosclerotic bone lesion is obscure. It has certain resemblances to generalized osteoporosis in that it is twice as frequent in females as in males. Pregnancy seems to have an accelerating effect on the progressive hearing loss of stapedial and otosclerosis in 25 per cent of cases while puberty and the menopause seem to have a similar but less pronounced effect. Heredity probably also plays a role since 50 per cent of patients with stapedial otosclerosis have one or more blood relatives with the condition.

The histologic bone lesion has been compared to young callus bone in the healing of fractures. It has also been compared to Paget's disease. In both conditions as in the active stage of otosclerosis there is vigorous remodelling activity with irregularly arranged lamellae of bone separated by numerous vascular spaces rich in osteoblasts and osteoclasts. In Paget's there is little or no tendency towards maturation and there is diminished remodelling activity, while in callus there is gradual progressive slowing of remodelling activity as calcium is deposited and the vascular spaces become filled with lamellar bone. Otosclerosis occupies a middle position between callus and osteitis deformans with its occasional but inconstant tendency toward recalcification to a more mature type of bone.

Schambaugh's experimental studies of the effect of fluoride on young bone and on experimental osteoporosis indicate that this ion retards the restoration phase of the remodelling cycle as the main effect with an additional calcification promoting effect. The dosage of sodium fluoride appeared critical. In treating patients with active otosclerosis and with Paget's disease, they utilized dosages of 30, 60 and 120 mg. per day. The 60 mg. daily dose appeared to be more effective than smaller or larger doses. They found as did other before them that patients with osteitis deformans feel better and have less bone pain when the 60 mg. daily dose is continued than when it is reduced after a time as recommended by Purves.³




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For patients with otosclerosis Schambaugh prescribes this dose in 20 mg. enteric coated tablets, one after each meal for a full year. Toxic effects other than occasional gastric irritation was practically non-existent. This is not surprising for we now know that the fluoride which is not deposited in bone is all excreted in the urine. In a very few patients with chronic arthritis, the joints become more painful while taking the medication but returned to their previous status when the medication was stopped. In no case did Schambaugh observe increased roentgenologic density of skeleton.

We know already that a sufficient intake of fluoride is necessary in early life for the formation of caries resistant teeth. In the later years of life a higher intake of fluoride appears to be necessary also to maintain normal calcification of bone. The reason is that the principle action of fluoride on bone is slowing of the resorptive phase of the remodelling process with an additional promotion of recalcification.

Occasionally osteoporosis is induced by heparin, cortisone or fractures. In such clinical situations previous medication with fairly large doses of sodium fluoride over a long period of time appears to be effective. When one of these forms of osteoporosis or localized osteoporosis of the labyrinthine capsule due to otosclerosis develops in a patient not so protected, the favorable effect of fluoride appears to be enhanced by simultaneous administration of phosphates as indicated by experiments in progress in Schambaugh's laboratory.

The time may not be far distant when fluoride will be recognized as essential to health, and when in addition to being added to the water supply, where it is deficient, it will also be prescribed to older persons to prevent senile osteoporosis and frequent fractures as well as those with otosclerosis to prevent progressive hearing loss.

L.H.N.

References

1. Schambaugh, Jr., G. E. and Petrovic, A.: Effect of sodium fluoride on bone. *JAMA*, 204: 969, June 10, 1968.
2. Guild, S. R.: Histologic otosclerosis. *Ann. Otol.*, 53: 246, 1944.
3. Purves, M. J.: Some effects of administering sodium fluoride to patients with Paget's disease. *Lancet*, 2: 1188, Dec., 1962.

Genetic Factors In Coronary Heart Disease

The risk factors in coronary heart disease (CHD) are now well publicised. Hypercholesterolemia is

in some way genetically controlled although it is subject to considerable influence by environmental factors. Thomas¹ studies showed a high incidence of CHD parents in students with high cholesterol levels. The same was true of Basset's² studies in parents of medical students who had high cholesterol levels. Regardless of the degree of genetic determinism here, the fact is that by appropriate diets and in some cases with the help of astromid-S hypercholesterolemia can be controlled.

Another risk factor is hypertension. Smirk and Hall³ by intensive breeding were able to develop several families in rats with a high incidence of hypertension. There is also a hypertensive strain in mice in which the mode of inheritance is poly-genetic. We are, of course not considering the variety of hypertensions caused by pheochromocytoma, aldosterone tumors, renal artery stenosis and chronic nephritis. At all events hypertension whether genetic or environmental is also generally manageable by medical means as well as surgery in the infrequent case requiring it.

Sex is recognized as a risk factor. The incidence of CHD in women before the menopause is considerably less than in men, provided they suffer from no other "risk" factor. After the menopause the incidence of CHD in women rises until they reach the age of 55-60 when CHD among men and women equalizes. The obvious suggestion seems to be to give estrogens to women after the menopause, in the hope of preventing increasing risk of developing CHD.

There are other risk factors also manageable medically such as diabetes, obesity and hyperuricemia, all of which may have some genetic determinant but which are now amenable to medical management. Body build, temperament and personality types have also received their share of attention, although the part played by inheritance in these areas requires much further study. There is, however, a need for basic and applied research in the field of genetics of CHD aside from the recognition and management of the "risk" factors.⁴

There are individuals who develop CHD in whom the disease cannot be correlated with levels of serum cholesterol, sex, diet or physical exercise or the presence of other risk factors. Clues to the genetic nature involved in the genesis of CHD are suggested by animal studies. Lofland and Clarkson⁵ found spontaneous atherosclerosis in certain breeds of pigeons in which only genetic background and age could be correlated with susceptibility to the disease. The incidence and severity could not be

correlated with some known risk factors in man such as serum cholesterol levels, sex, diet or physical exercise. However, cholesterol feeding of these breeds increase the incidence of atherosclerosis in accordance with the susceptibility of the breed even though no significant difference in serum cholesterol levels among the breeds occurred.

If this exists in some animal species, it could exist in man also. If there is a genetic contribution what could be the mechanisms by which the genetically determined susceptibility to CHD operate? Many mechanisms with regard to the "risk" factors have been incriminated. There is probably a genetic basis in the pattern of coronary artery anatomy. Certain kinds of patterns which allow for better collateral circulation could delay symptoms, but do not in themselves operate against atherogenesis. For example Schlesinger in his classic studies on coronary artery distribution over thirty years ago showed the protective effect on infarction of two posterior descending branches, one from the right and the other from the left coronary artery. Whether different anatomical patterns predispose to atherogenesis however requires further study.

Another possibility is the existence of a defective genetically determined fibrinolytic enzyme system in man, as revealed in the studies by Cash in Edinburgh.⁶ This system is believed to be in a

state of dynamic flux. Some individuals show a defect not apparent from measurements of absolute resting levels of plasminogen activator. If fibrin deposition on arteries leads to atherosclerosis as some investigators believe,⁷ then a defective fibrinolytic system could very well predispose to atherogenesis.

If we knew how to detect the genetically susceptible individual perhaps we could apply appropriate preventive measures. Perhaps also we might get to understand the genetic mechanisms which determine the increased vulnerability. This should lead to devise methods for breaking the chain leading to CHD, as we are now able to do so well with the "risk" factors.

L.H.N.

References


1. Thomas, C. B.: Observations on some possible precursors of essential hypertension and coronary artery disease: V. Hypercholesterolemia in healthy young adults. *Am. J. Med. Sci.*, 232: 389, 1956.
2. Basset, D. R.: Serum lipids in young males with parental atherosclerosis. *Am. J. Med. Sci.*, 243: 740, 1962.
3. Smirk, F. H. and Hall, W. H.: Inherited hypertension in rats. *Nature*, 182: 727, 1958.
4. Bloor, C. M. and McKusick, V. A.: The genetics of coronary artery disease. Symposium on coronary heart disease. *Am. Ht. Assoc. Monograph Number Two*. New York, 1968.
5. Loffland, H. B. and Clarkson, T. B.: A biochemical study of spontaneous atherosclerosis in pigeons. *Circulation Research*, 7: 234, 1959.
6. Cash, J. D.: A new approach to studies of the fibrinolytic enzyme system in man. *Am. Ht. J.*, 75: 424, March 1968.
7. Duguid, J. B.: Thrombosis as a factor in the pathogenesis of coronary atherosclerosis. *J. Path. and Bact.*, 58: 207, 1946.

Some Bizarre Legal Decisions In Workmen's Compensation For Heart Disease

Heart cases will continue to remain a troublesome legal problem as long as some physicians state emphatically that effort and exertion have nothing to do with myocardial infarction, while others base their position on the opposite thought. Thus the reason for litigation in the cases of coronary heart disease is referred to differences of opinion within the medical profession. Without doubt medical disagreement has also contributed to skepticism of the legal profession and their wish to remain adversaries, rather than to depend on panels and "impartial physicians." We must, of course, not minimize a certain apprehension on the part of some lawyers that if "impartial physicians" decide medical matters for the courts, that litigation may diminish.

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Liability usually holds, if during unusual exertion, something "lets go" such as hernia, cerebral hemorrhage, blood vessel rupture, including aneurysms and apoplexy although many of these are in doubtful relation to a strain. In cases of myocardial infarction, dilatation of the heart, and even arteriosclerosis occurring during routine exertion, the courts have been far less definite. In the cardiac field a major legal tussle often takes place over the point as to whether or not an unusual degree of stress has occurred to precipitate the attack.¹

In Georgia for example heart failure has been held to be an accident even when the exertion was lighter than usual as long as it was "considered" to have precipitated the attack. The courts in that state have carried its legal conclusion to the ultimate stage by holding that "an accident arises out of employment when the required exertion producing the accident is too great for the man undertaking the work whatever the degree of exertion or condition of health." This principle is accepted in New York since the Masse case (1950) when it was held that "whether or not a particular event is an industrial accident is to be determined not by any legal definition but by the common sense viewpoint of the average man."

There is a fear in the part of Workmen's Compensation Board and the courts that heart cases will get out of control and this sets some arbitrary boundaries for their decisions. One senses that they would really not want to compensate for deaths not actually caused in any substantive degree by employment. In general there must be an unexpected result and there must be some exertion capable of medically causing collapse. Nevertheless, Chief Justice Bragg in Massachusetts held "acceleration of previously existing heart disease to a mortal end is an injury within the meaning of the Workman's Compensation Act."^{2, 3}

We physicians must view some of these decisions with amazement. In one case a man fractured a heel bone in a fall and was said to have had pain and to have been anxious. He died three months later of a myocardial infarct. Only one of five doctors thought there was a connection but the Board chose this one's opinion and held for the plaintiff! In another instance a judgement was given for the plaintiff on the basis that a myocardial infarct allegedly due to lifting lowered his "resistance" so that he died of cancer of the bladder. Courts have found for the plaintiff when he suffered an attack during an altercation in which he was the aggressor.

Medical testimony may be completely ignored by the court and it is true that appeal boards tend to uphold Compensation Boards even in the absence of a "single shred" of medical evidence of causal relation.⁴ A truck driver may work long hours without regular sleep and gain forty pounds in weight, yet if he has a heart attack the decision may imply that the work alone was the cause of his death. "Presumption as to cause," says a Tennessee Court "should be resolved in favor of the employee." In Massachusetts the principle of emotional stress was held valid for the death of a motor vehicle inspector from a coronary attack occurring one to two hours after a supposedly stressful interview with the survivor of an accident, without any testimony that the interview was emotionally disturbing. The Supreme Court merely decided it must have been!

Many cases are being decided in favor of the claimant whose heart attack has been found casually related to emotional stress. While sudden death from an acute emotional episode undoubtedly occurs, the Michigan Supreme Court "has treated the emotional pressures arising from ordinary work as mental stimuli sufficient to produce a compensable injury."¹ It is but a short step from fright, prolonged over a period of time, to continued worry and anxiety. One such case with judgment for the claimant concerned a woman bookkeeper with hypertension, feelings of insecurity and family problems who became upset when her accounts did not balance and suffered a heart attack.

In the Supreme Court of the State of Washington a judgment was ordered for the plaintiff's heirs because he was found dead forty minutes after the end of his working day during which he pulled levers. A physician had testified that "the fatal attack was precipitated by some physical activity which caused the clot, shown to be of duration to get loose!"⁵ At autopsy a right coronary artery was shown to be occluded by a thrombus. Is there any wonder such evidence makes high court pronouncements about causation meaningless. Evidence of likelihood has become enough in some courts.

Bugaboos thus become precedents as in a Tennessee case "the court takes judicial notice that climbing of stairs is condemned by the medical profession as among the activities most harmful and dangerous to persons afflicted with heart trouble or arteriosclerosis"! This superstition about danger of mounting stairs to cardiac patients is only matched by the one which holds raising arms over the head is a fearful act.

The concept that occupation as such, especially the so-called emotionally stressful ones are responsible for coronary heart disease and atherosclerosis is entirely lacking in proof. Ryan and Moritz⁶ state that "in no circumstances can stress or injury be held accountable for coronary atherosclerosis." There was a time when a great cult of stress was built up in this country aided by reports that under conditions of emotional pressure serum cholesterol rises and coronary trouble ensues. Goffman⁷ has recently shown that in one of these studies the rise in serum cholesterol was completely explicable on the basis of the admitted fact that the victims (accountants) under stress also ate more! This idea is fortunately coming to rest since it has been shown that physical activity actually reduces serum cholesterol.⁸ There would appear to be more evidence now that energetic stressful reactive life has in fact protective value. However, since it is impossible to titrate emotional stress, any conclusions of "stress" studies are largely meaningless.

In the field of Workmen's Compensation one cannot disregard the pressure to include degenerative diseases in compensation injuries simply on the basis of social desires. It is to be hoped that some solution will be reached since not only is the potential liability for coronary disease enormous in the American pattern of life but the need for rehabilitation and employment of cardiac subjects and older workers demands a clear cut classification. Either coronary heart disease is to be considered occupational and included in Workmen's Compensation, or it should be provided for by some of sickness disability insurance realizing that there will be encountered difficulties in either solution.

L.H.N.

References

1. Sprague, H. B.: Legal aspects of coronary disease. Symposium on coronary heart disease. (Second edition-revised) Am. Ht. Assoc. Monograph No. 2. Edited by Herrman L. Blumgart, American Heart Association, Inc., New York, 1968.
2. Brightmans Case Mass Reports (220 Mass 17) 1914.
3. Clark, R. J., Toussant, E. S. and Sprague, H. B.: Heart disease in Massachusetts in relation to the Workmen's Compensation Act. New Eng. J. Med., 252: 478, 1955.
4. NACCALJ, 12: 87, Nov., 1953.
5. NACCALJ, 11: 75, May, 1953.
6. Regan, S. J. and Moritz, A. R.: Handbook of legal medicine. C. V. Mosby Co., St. Louis, 1956, p. 125.
7. Goffman, J. W.: Coronary heart disease. Charles C. Thomas, Springfield, Illinois, 1959.
8. Nahum, L. H.: Exercise and coronary heart disease. Conn. Med., to be published.

Alpha-Methyl Dopa Induced Hemolytic Anemia

Recent observations indicate that a number of adverse reactions affecting the human erythrocyte proceed by immune mechanisms. Such immune mechanisms are recognized and studied by the Coombs' test. The Coombs' is an antiglobulin test for the demonstration of antibody attachment to the erythrocytes. It appears that there are two major coatings of red cells with proteins. If the red cells acquire their coatings in vivo, that are circulating in the coated state, the antiglobulin test is referred to as a positive direct test. If the technic is used to detect in vitro sensitization of red cells by serum antibodies or complement, then the test is referred to as the indirect test.

With the Coombs' positive test there has developed considerable knowledge about hemolytic anemias that develop after the administration of certain drugs such as penicillin, quinine and alpha-methyl dopa used frequently in the treatment of hypertension. The relation of alpha-methyl dopa to hemolytic anemia became apparent during the first half of 1966, through a series of letters to the editor of *Lancet*. Carstairs, et al^{1, 2} found 20 per cent of patients taking the drug to have a positive direct IgG Coombs' test. While these patients did not show anemia as yet they developed the positive test after taking the drug for five months to one year and probably would have developed anemia if ingestion of the drug were continued or its dose increased. Their further studies on 25 of 30 patients with Coombs' positive hemolytic anemia after taking alpha-methyl dopa five to thirty-seven months revealed that the anemia promptly responded to drug withdrawal although the positive Coombs' test persisted for much longer.

Croft, et al³ case was that of a 60 year old woman who developed anemia after taking alpha-methyl dopa for seven months in one gram per day doses. She also recovered completely from her anemia six weeks after discontinuing the drug. The precise role of the drug in the pathogenesis of the erythrocyte autosensitization is unclear. At present there is no evidence that alpha-methyl dopa or various metabolites can inhibit or enhance the reactivity of normal red cells. What is clear from Croft's report is that the immunologic mechanisms in this form of hemolytic anemia are distinct from those associated with penicillin hemolytic anemia or that resulting from quinine or stibophen.

The hemolytic anemia associated with alpha-methyl dopa therapy presents a unique opportunity to learn more about the obscure mechanisms in autoimmune hemolytic anemia and in fact in autoimmunity in general. The existence of this syndrome emphasizes the need to obtain a detailed drug history from patients with such disorders. In time through diligent observation more cases of so-called "idiopathic" autoimmune hemolytic anemia may be recognized to be associated with environmental agents.

The mechanism by which red cells are affected are now known to be several. There are some immune reactions affecting red cells involving antibodies that can directly agglutinate or in some cases directly lyse red cells. In this case one can recognize intravascular hemolysis with hemoglobinemia and hemoglobinuria. Other immune reactions involving red cells lead to coating of the cells with antibody or complement protein or both without producing direct agglutination or direct lysis. The immune reactions initiated by penicillin, quinine and alpha-methyl dopa are of this type, that is involving sensitization of erythrocytes with antibody (gamma-G-globulin) or complement. How then does the red cell develop a shortened survival?

There are several consequences of the interaction between the sensitized red cells and the reticuloendothelial system and the spleen. One is phagocytosis, another is removal from the red cell of small portions of its cell membrane. As a result of this distortion the life span of the cell is greatly shortened. There is finally the mechanical trauma of the splenic circulation alone with its tortuous narrow passageways which may lead to lysis of some damaged erythrocytes. These three mechanisms certainly could operate together in varying degrees in cases of erythrocyte sensitization by antibodies that are non hemolytic in vitro.

We need to remember that new drugs will continue to be introduced into clinical medicine and undoubtedly a few will have a potentiality for producing reactions like those from alpha-methyl dopa. Periodic antiglobulin tests might be carried out as a part of the screening of new drugs particularly as they enter wide clinical use. Such screening could give powerful insights into the pathogenesis of autoimmune hemolytic disease, beside the obvious degree of safety it would afford the physician in drug administration. The red cell is easy to study serologically and we already know a good deal about its involvement in drug related immune processes.

There is good evidence that platelets as well are subject to at least some of these reactions. It may be that similar processes can involve the less easily studied leucocytes and possibly the bone marrow itself and even a wide range of other tissues.

L.H.N.

References

1. Carstairs, K. C., Breckenridge, A. Dollery, C. T. and Worledge, S. M.: Incidence of a positive direct Coombs' test in patients on alpha-methyl dopa. *Lancet*, 2: 133, 1966.
2. Worledge, S. M., Carstairs, K. C. and Dacie, J. V.: Auto-immune haemolytic anemia associated with alpha-methyl dopa. *Ibid.* p. 135.
3. Croft, J. D., Jr., et al: Coombs' test positivity induced by drugs: mechanisms of immunologic reactions and red cell destruction. *Ann. Int. Med.*, 68: 176, 1968.

Letter To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Dr. Nahum:

I have read and enjoyed your recent four editorials on the problems and challenges of modern dentistry and dental research. Your statement that there may be implications to bacteremia other than endocarditis is most certainly true.

I have enclosed a recent reprint about this problem. Although this is the only report of its kind to date, I suspect that others will follow. My own current study of oral cellulitis secondary to dental infection reveals that 8 per cent are now gram-negative in nature.

Again, thank you for your interest in dental problems.

Sincerely,

Morton H. Goldberg, D.M.D., M.D.

60 Gillett Street, Hartford, Connecticut

177th ANNUAL MEETING
CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel
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May 13, 14, 15, 1969

PRELIMINARY PROGRAM
TUESDAY, MAY 13

MORNING SESSION

ANNUAL MEETING OF THE HOUSE OF DELEGATES
OPENING SESSION

TERRACE ROOM —:— MEZZANINE

- Kenneth F. Brandon, Hartford, Conn., Speaker of the House, presiding
Frank K. Abbot, Waterbury, Conn., Vice-Speaker of the House
- 8:00 REGISTRATION OF DELEGATES
Continental Breakfast for Delegates and Official Guests
- 8:30 CALL TO ORDER
- 11:45 REFERENCE COMMITTEE HEARINGS—Cities Room—Mezzanine
- 12:30 LUNCHEON FOR DELEGATES AND OFFICIAL GUESTS—Fourth Floor Rooms

TUESDAY, MAY 13
SCIENTIFIC PROGRAMS

AFTERNOON SESSION

- 1:00 REGISTRATION—Mezzanine
OPENING OF EXHIBITS—Ballroom—Mezzanine

TERRACE ROOM

- 1:30 CALL TO ORDER—ADDRESS OF WELCOME
Norman H. Gardner, East Hampton, Conn., President of the Society

PANEL ON MEDICAL, BEHAVIORAL, ENDOCRINE
PROBLEMS IN ADOLESCENTS

- Moderator: Walter R. Anyan, Jr., New Haven, Conn.
- 1:45 SEX PROBLEMS AND EDUCATION OF ADOLESCENTS: SCOPE AND METHODS
Mary S. Calderone, New York City
- 2:20 DRUG USE, ABUSE AND DEPENDENCY IN THE ADOLESCENT PERIOD
Charles Clay Dahlberg, New York City
- 2:55 DISCUSSION—Questions and Answers
DISCUSSANT: J. Roswell Gallagher, New Haven, Conn.
- 3:30 INTERMISSION TO VISIT TECHNICAL EXHIBITS
- 4:00 SECTION MEETINGS

Tuesday, May 13

EVENING SESSION

- 6:30 RECEPTION AND DINNER FOR DELEGATES AND OFFICIAL GUESTS
Cities Room, Mezzanine
- 8:00 PROGRAM ON STUDENTS IN REBELLION—Terrace Room
Moderator: Roswell D. Johnson, Director, Brown University Health
Services, Providence, Rhode Island
Panelists: Mr. William C. French, Superintendent of Schools, New
Canaan, Connecticut
Mr. John C. Esty, Jr., Headmaster, Taft School, Water-
town, Connecticut
Mr. Henry Coleman, Dean of Freshmen, Columbia Col-
lege, New York, City

WEDNESDAY, MAY 14

MORNING SESSION

HOUSE OF DELEGATES

FINAL SESSION

TERRACE ROOM —:— MEZZANINE

- 8:00 REGISTRATION OF DELEGATES
Continental Breakfast for Delegates and Official Guests
- 8.30 CALL TO ORDER
- 12:30 ADJOURNMENT

Wednesday, May 14

SCIENTIFIC PROGRAM

MORNING SESSION

- 9:00 REGISTRATION—Mezzanine

ROUND TABLE DISCUSSIONS

- 10:00-11:30 Fourth Floor in Rooms Designated
PITFALL IN INTERPRETING ELECTROCARDIOGRAMS—Room-424
Group Leader: Edgar Lichstein, New Britain, Conn.
EVALUATION OF COAGULATION DISORDERS—Room-420
Group Leader: Stuart C. Finch, New Haven, Conn.
NEW CONCEPTS IN PATHOGENESIS AND TREATMENT OF DIABETIC STATE—
Room-416
Group Leader: David S. Wilcox, Hartford, Conn.
NEW MANAGEMENT OF RH INCOMPATIBILITY—Room-412
Group Leader: John T. Queenan, Greenwich, Conn.
- 11:30 INTERMISSION TO VISIT TECHNICAL EXHIBITS
- 12:30 LUNCHEON—Cities Rooms

Wednesday, May 14
AFTERNOON SESSION

TERRACE ROOM

SYMPOSIUM ON CURRENT TECHNIQUES IN THE MANAGEMENT OF
MYOCARDIAL INFARCTION

Presiding: Howard Levine, New Britain, Conn.

- 1:30 CORONARY CARE EXPERIENCES AND FUTURE DIRECTIONS
James K. Cooper, Arlington, Virginia
- 2:00 NEW AND OLD DRUGS IN THE TREATMENT OF MYOCARDIAL INFARCTION AND
ITS COMPLICATIONS
Edmund H. Sonnenblick, Boston, Mass.
- 2:30 NEW ELECTRONIC AID IN THE MANAGEMENT OF MYOCARDIAL INFARCTION
AND ITS COMPLICATIONS
Leslie A. Kuhn, New York City
- 3:00 DISCUSSION—Question and Answers
- 3:30 INTERMISSION TO VISIT TECHNICAL EXHIBITS
- 4:00 SECTION MEETINGS

EVENING PROGRAM

- 6:15 RECEPTION—Mezzanine
- 7:00 ANNUAL DINNER OF THE SOCIETY—Terrace Room

THURSDAY, MAY 15
SCIENTIFIC PROGRAMS

MORNING SESSION

- 9:00 REGISTRATION—Mezzanine

ROUND TABLE DISCUSSIONS

- 9:30-10:30 Fourth Floor in Rooms Designated
- FACIAL PAIN—Room-424
Group Leader: Lewis L. Levy, New Haven, Conn.
- MANAGEMENT OF BREAST METASTASES—Room-420
Group Leader: Ira S. Goldenberg, New Haven, Conn.
- EVALUATION OF HEARING DISORDERS—Room-416
Group Leader: David S. Green, Ph.D., New Haven, Conn.
- TRAUMA TO THE HAND—Room-412
Group Leaders: Kristaps J. Keggi, New Haven, Conn.
James A. Albright, New Haven, Conn.
- 10:30 INTERMISSION TO VISIT TECHNICAL EXHIBITS

TERRACE ROOM

PANEL ON ORGAN VISUALIZATION

Presiding: William F. Eckhardt, Jr., New Canaan, Conn.

- 11:00 NEWER DYNAMIC TECHNIQUES (Brain and Heart)
Merrill A. Bender, Buffalo, New York
- 11:30 CURRENT STATUS OF RADIOISOTOPES SCANNING
Henry N. Wagner, Jr., Baltimore, Maryland
- 12:00 DISCUSSION—Questions and Answers
- 12:30 LUNCHEON—Cities Rooms
- INTERMISSION TO VISIT TECHNICAL EXHIBITS

Thursday, May 15
AFTERNOON SESSION
TERRACE ROOM
PANEL ON ARTERIOGRAPHY

Moderator: Jack L. Westcott, Hartford, Conn.

- 1:30 WHY AN ANGIOGRAM?
Douglas F. Adams, Boston, Massachusetts
- 2:00 RECENT ADVANCES IN ABDOMINAL ARTERIOGRAPHY
Stanley Baum, Philadelphia, Pennsylvania
- 2:30 DISCUSSION—Questions and Answers
- 3:00 INTERMISSION TO VISIT TECHNICAL EXHIBITS
- 3:30 PROGRAM ARRANGED WITH THE CONNECTICUT SOCIETY OF AMERICAN BOARD
SURGEONS
- 4:00 SECTION MEETINGS
-

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Electrical Conversion of Arrhythmias Under Diazepam Sedation

Wallace B. Lebowitz, M.D.

Introduction

Precordial electric shock for the termination of arrhythmias is uncomfortable in the conscious patient.¹⁻³ The use of transient narcosis is, therefore, favored.⁴ Thiopental sodium has been widely employed for this purpose,^{5,6} however, administration of this drug requires the presence of an anesthesiologist, and the scheduling of a medical therapy with the surgical department. In addition, general anesthesia in ill patients with heart disease has its hazards and practical problems.^{4,6} Recently, diazepam*, a psychotherapeutic agent, has been suggested for this purpose.^{7,8} This agent seemed to hold promise to us and, hence, an investigation of the effectiveness of intravenous diazepam as sedation-analgesia for elective or emergency electrical conversion of arrhythmias was undertaken.

Materials and Method

Sixty-seven electric countershock treatments were performed on 50 patients, including 21 males and 29 females with a mean age of 60.8 (37 to 79) years. Eleven patients were treated more than once.

Diagnoses included arteriosclerotic heart disease in 34, rheumatic heart disease in 14, ASHD and RHD in 1, and mitral regurgitation secondary to ruptured chordae tendineae in one. Seven patients had had recent cardiac surgery, 8 had had acute myocardial infarctions, 15 patients were in congestive heart failure and 6 had cardiogenic shock. Several patients had had drug therapy of their arrhythmias previously without improvement.

A total of 42 elective and 25 emergency procedures were performed for: atrial flutter (29 times), atrial fibrillation (24 times), ventricular tachycardia (10 times), and paroxysmal atrial tachycardia (4 times).

All procedures were performed in the hospital's intensive care unit. Where possible, nonessential

medications, including tranquilizers, were omitted prior to electric shock therapy. Resuscitative equipment and drugs were at bedside in each case.

The compound was instilled slowly, intravenously, immediately before the electric shock was applied. The patient was engaged in conversation, and when speech became slurred, 15-30 sec was allowed to pass before an additional 2-3 mg was given, if needed. The final dosage varied from 5-30 mg with a mean of 14.8 mg.

Synchronized direct current shock was used in all instances. Continuous blood pressure and electrocardiographic monitoring was carried out before, during and after the application of the shock. A record was kept of the response to the shock, the time to recover complete alertness, the subsequent degree of amnesia for the event and the occurrence of side effects and/or unusual reactions.

Results

All patients experienced a variable degree of hypnosis within 2-3 minutes. One patient with cardiogenic shock developed transient apnea and required assisted ventilation for approximately 3 minutes. Another developed Cheyne-Stokes respiration, which was promptly reversed with intravenous aminophylline. No other instance of respiratory depression was encountered. Reduction of mean blood pressure varied from 2-10 mmHg and in no patient was it considered significant. Two patients experienced mild depressive reactions after awakening with intermittent sobbing lasting from 5-15 minutes. No other side effects of the drug were noted.

Maximal electric current applied to each patient varied from 20 to 400 watt-seconds. One shock was required 14 times, 2 shocks 29 times, 3 shocks 21 times, and 4 shocks 3 times. Successive shocks were applied within 30 sec to 2 min of each other. Muscular twitching or slight movement was noted on 57 instances while arousal occurred 10 times. Pain was not observed with 55 shocks while a variable degree of pain was noted 12 times. Amnesia for the shock was complete on 58 occasions, marked on 6 and mild to moderate in 3. All patients experiencing pain had subsequent amnesia for the event.

From the Cardiovascular Laboratory, St. Vincent's Hospital, Bridgeport, Connecticut.

DR. WALLACE B. LEBOWITZ, Associate Attending Cardiologist and Director, Cardiovascular Laboratory, St. Vincent's Hospital, Bridgeport.

* Hoffman-LaRoche, Inc., Nutley, New Jersey.

Successful conversion of the arrhythmia was accomplished in 63 of 67 instances. The arrhythmia in 1 patient with myocardial infarction and cardiogenic shock was successfully terminated, but the patient died 1 hour later from his basic disease. No other death occurred.

Return to complete alertness occurred within 15 to 180 minutes from the time the drug was administered, although the majority began to awaken within 5 to 15 min. Less apprehension was noted following the conversion attempt in all patients.

Discussion

Although some investigators feel that anesthesia is not necessary,⁹ the degree of apprehension in some patients, the variation in pain threshold in other patients and the increasing pain with multiple shocks of increasing intensity make anesthesia and/or analgesia desirable.⁴⁻⁶

Thiopental sodium was routinely employed in our hospital prior to this study. The anesthetic had generally proved safe and effective for this purpose, however, as others had observed,^{5,6} premature ventricular contractions occurred frequently with its administration. These ventricular premature beats are potentially hazardous since the subsequent countershock may be applied during the succeeding ventricular vulnerable phase.¹⁰

In this investigation, diazepam was employed safely and successfully in patients undergoing electrical termination of arrhythmias. The degree of sedation and analgesia-amnesia produced by diazepam intravenously, was found to be quite suitable for direct current countershock. Moreover, no premature contractions were observed with administration of the drug.

The use of thiopental sodium or other anesthetics during electric countershock therapy requires the presence of an anesthesiologist and the performance of a medical therapy in the surgical area of the hospital.

With diazepam, all of our procedures were carried out in the hospital's intensive care unit and on no occasion was the presence of an anesthesiologist required. Time-consuming preparation of the patient and scheduling of a medical procedure with the surgical department were also obviated.

The drug was generally well-tolerated and those side effects that were encountered occurred either with too rapid administration of the drug or in patients with cardiogenic shock. Diazepam, intra-

venously, must therefore be given slowly to prevent exceeding the lowest possible dosage that will give the required sedation. In addition, if administered to patients with cardiogenic shock, it should be given very slowly, in low dosage and with extreme caution.

When administered properly, however, intravenous diazepam is a satisfactory therapeutic agent for use during elective or emergency electrical termination of cardiac arrhythmias.

Summary

The effectiveness of intravenous diazepam as sedation-analgesia for electrical termination of 67 cardiac arrhythmias in 50 patients was investigated. Satisfactory hypnosis and analgesia-amnesia were obtained during high voltage electric countershock therapy.

All procedures were safely performed in the intensive care unit without the need of attendant anesthesiologist. The results of this study indicate that intravenous diazepam is a satisfactory agent for use in patients undergoing electrical termination of cardiac arrhythmias.

Acknowledgement

The technical assistance of N. Francisco, M.D. and D. Monakil, M.D. is gratefully acknowledged. Carolinn Homp, R.N., prepared the manuscript. Diazepam (Valium) was supplied by Hoffman-La Roche, Inc., Nutley, New Jersey.

References

1. Lown, B., Amarasingham, R. and Neuman, J.: New method for terminating cardiac arrhythmias. *J.A.M.R.*, 182: 548, 1962.
2. Zoll, P. M., Paul, M., Linenthal, A., Norman, L. and Gibson, W.: The effects of external currents on the heart. *Circulation* 14: 745, 1956.
3. Zoll, P. M. and Linenthal, A. J.: AC and DC countershock for arrhythmias. *J.A.M.A.* 188: 327, 1964.
4. Paulk, Jr., E. A. and Hurst, J. W.: Clinical problems of cardioversion. *Amer. Heart. J.* 70: 259, 1965.
5. Shephard, D. A. E. and Vandam, L. D.: Anesthesia for cardioversion. *Amer. J. Card.* 15: 55, 1965.
6. Lundberg, R. O., Sessler, A. D. and Moffitt, E.: Anesthesia in clinical cardiac laboratory. *Surg. Clin. N. Amer.* 4: 868, 1965.
7. Nutter, D. O. and Massumi, R. A. Diazepam in cardioversion. *New Eng. J. Med.* 273: 650, 1965.
8. Kernohan, R. J.: Diazepam in cardioversion. *Lancet* 1: 718, 1966.
9. Stock, R. J. and Lown, B.: Correspondence. *New Eng. J. Med.* 269: 534, 1963.
10. Muenster, J. J., Rosenberg, M. S., Carleton, R. A. and Graettinger, J. S.: Comparison between diazepam and sodium thiopental during DC countershock. *J.A.M.A.* 199: 758, 1967.

Cervical Cancer Detection Employing The Vaginal Irrigation Smear Technique

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Carcinoma of the cervix ranks second only to carcinoma of the breast as a cause of death from cancer among women. Over 10,000 women die from this disease each year in the United States. With the advent of cytological smears, this disease should be almost entirely preventable, yet only 15% of adult American women are currently being screened. The irrigation smear technique offers new hope for reaching more women for routine screening. Because cervical carcinoma is relatively asymptomatic in the early stages, women are not motivated sufficiently to obtain yearly gynecological examinations. Any method with significant accuracy which can be utilized to screen large numbers of women has a definite place in the control of this disease. The vaginal irrigation smear technique which was developed by Davis² is simple to obtain, does not require medical assistance for obtaining specimens and is relatively inexpensive.

Even its strongest supporters do not advocate it as a replacement for yearly gynecological exams but offer it as an adjunct for screening larger numbers of women than are presently being done. The import on communities where this has been tried has not been a decrease in physician office visits, but rather a two fold increase in women appearing for office examinations. An obvious increased awareness by both physicians and patients of the value of routine physical exams and cytological studies was noted. Women who had not previously been examined by any method were ferreted out and positive and suspected cases brought to medical attention. A pilot study in Washington County revealed that 5% of women in that locale were having annual PAP smears. With the cooperation of the local Medical Society, local newspapers, and civic groups 80% of women between the age of 30 and 45 were motivated to participate in a mailing campaign of vaginal irrigation smears.¹ A similar

campaign in Denmark had an initial 77% response with a subsequent 5.2% additional response on second request. Newspaper and T.V. media were utilized to support this mailing campaign.⁵ The Bell Telephone Company, with enthusiastic support from management, obtained a 92.3% return rate. In a series of 1,200 women, six cases of cervical carcinoma were diagnosed by the vaginal irrigation technique, one of which had been missed by cervical scraping.⁴ Other mailing campaigns without radio, T.V. and civic group support met with a 30-40% return rate.⁶

A critical evaluation of the vaginal irrigation smear technique was carried out by Davis in 1962.³ In a series of 1,000 patients with no other clinical information other than the date of the last menstrual period available at the time of cytological reading, questionable or positive results were obtained in 122 of 127 cases of pre invasive and invasive Ca. These were controlled by gynecological exam, Schiller test, punch biopsy and additional curettage or cone biopsy as clinically indicated. The diagnostic accuracy obtained in this study was 96% which compares well with conventional PAP scrape smears—Davis attributes this high degree of accuracy to the natural exfoliate tendency of most cervical cancers and to strict adherence to adequate slide preparation for final microscopic interpretation.

The V.I.S. technique utilizes a small soft plastic pipette with an irrigating fluid for vaginal lavage contained in its bulb. Collection may be accomplished by the patient or by nursing personnel. Instructions accompanying the pipette are simple and require no more skill than ordinary douching. The cap is removed from the pipette, and the stem inserted into the vagina. The patient then squeezes the bulb to distribute the irrigating fluid into the vaginal pool. The bulb is then released aspirating the lavaged exfoliated cells into the bulb. The pipette is removed, capped and sent to the laboratory for further fixing and slide preparation.

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The preparation and reading of V.I.S. slides differs from that employed in the conventional spatula scrape specimens and will be briefly described.

The bulb of the V.I.S. pipette which contains the partially fixed aspirated cells from the vaginal pool is centrifuged briefly in a standard centrifuge. Excess supernate is then poured off leaving a concentrated solution of cells. These are then fixed with an equal volume of a mixture of alcohol, ether, and glacial acetic acid. This fixing process is repeated again and after a third centrifuging the fixative is completely decanted and a single drop of sediment is placed on a slide using the tube of the V.I.S. pipette to obtain the specimen. The sediment is then smeared in a monolayer with the side of the stem which has a screened area for this purpose. Excess sediment is then resuspended in saline and alcohol so that additional slides may be prepared if desired. Air drying yields a uniform monolayer of cells which are markedly adherent to the glass slide and easily stained for reading utilizing the standard Papanicolaou's method. Cover slips are then applied in the usual manner.

The actual reading of the V.I.S. slides differs somewhat from the cervical scrape method in that a uniform monolayer of 50,000 to 100,000 cells are available for screening with less tendency to clumping. Also, the staining characteristic differs somewhat, probably due to differences in the method of fixations previously described.

The Vaginal Irrigation Smear Technique has been recently employed in the Greater Hartford, Connecticut area. Exfoliated cervical cells are collected by irrigating the vaginal pool with a disposable, soft plastic pipette containing fixative and preservative solutions. Samples are self-obtained by the patient and require no more skill than douching.

The following is a report of our first 1,000 V.I.S.:

Approximately 50% of women in this series had routine PAP smears within a two year period prior to the V.I.S. There were twenty suspicious or posi-

tive smears, all of which were followed up with physician-obtained cervical scrape smears and pelvic exams. Of these, four proved to be positive, two of these had previous PAP smears and two did not. The rate of 4 per 1,000 positive smears compares well with the rate of 3 to 4 per thousand noted at both cytology laboratories in this city.

Summary and Conclusions

With the advent of cytological screening, Carcinoma of the cervix should be virtually a preventable disease; yet it still remains a major health hazard. Any method which can improve the outlook of this disease has a place in its control. The Hartford area has a high rate of PAP Smear (Approximately 50%) yet four cases of Ca in Situ were detected by the Vaginal Irrigation Smear Technique. Industries employing large numbers of women, civic groups and visiting nurse organizations have been a source of significant yield in this project. It is our opinion that the Vaginal Irrigation Smear Technique is a valuable supplement for mass screening of Carcinoma of the cervix. Its relatively low cost, ease of specimen collection, and wider range of distribution are factors favoring more widespread use of this method as a supplement and not a replacement of present screening methods.

Studies utilizing technicians specially trained in interpreting V.I.S. slides in which strict adherence to collection, and preparation of adequate numbers of cells for cytological reading have been adhered to have attained a high degree of accuracy.

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References

1. Davis H. J.: An Epitaph for Cervical Carcinoma. Maryland State Department Health Bulletin: 1-6 Vol 36 June, 1964.
2. Davis H. J.: The Irrigation Smear: A Cytologic Method for Mass Population Screening by Mail. Am. Journal of Obstetrics and Gynecology. 84: 1017-1023, 1962.
3. Davis H. J.: The Irrigation Smear: Accuracy in Detection of Cervical Cancer Acta-Cytologica, Vol., No. 5, 459-467, Sept.-Oct., 1962.
4. Hilker R. J. et al: Uterine Cancer Detection Ca. Vol. 16, No. 1, 31-32, 1966.
5. Koch, F. and Stakemann, G.: A Population Screening for Carcinoma Of The Uterus With The Irrigation Smear Technique, Dan. Med. Bull. Vol 11, 201-213, 1964.
6. MacGregor, J. E. et al: The Cytopipette in the Diagnosis of Early Cervical Carcinoma. Lancet Vol. 1, 252-256, 1966.

Case No.	Irrigation Smear	Repeat Irr. Smear	Cervical Scrape	Previous	
				Cervical Scrape	Biopsy
151	Positive	—	IV	I	Ca. in Situ
236	Suspicious	Positive	—	None	Ca. in Situ
				Nine yrs.	
436	Suspicious	Suspicious	III	prior	Ca. in Situ
459	Positive	—	III	II	Ca. in Situ

First Annual Report on the Results of Intensive Coronary Care at the Greenwich Hospital Association

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Synopsis-Abstract

After one year of operation, the experience of a community hospital coronary intensive care unit (CICU) is reviewed. Seventy-one patients with the established diagnosis of acute myocardial infarction were admitted to this facility where they were treated aggressively for their disease. Although the mortality remained at 30%, it is evident that selection of "poor risk" patients for intensive coronary care was responsible for this unusually high figure. An analysis of the causes of death in the CICU revealed that 14 patients died of cardiogenic shock, six of intractable heart failure, and only one of an arrhythmia. Since it is generally accepted that electrical failure is the major cause of death in the first few days following an acute myocardial infarction, it is felt that the aggressive coronary care rendered in this facility represented a significant improvement in the care of these patients.

Acute myocardial infarction is the leading single cause of death in the United States, both in the elderly and in those below the age of 65.¹ There are 7,000 to 10,000 Americans who become victims of this disease each day, and some 1,500 of these die each day. The incredible fact that 3 million acute myocardial infarctions are recorded each year makes this one of the most urgent public health problems.^{1,2}

In 700 male patients suffering from acute myocardial infarctions at the University of Pennsylvania, it was found by Drs. Meltzer and Kitchell³ that 70% of the deaths from this disease occurred in the first five days; and, furthermore, 47% of these victims died of electrical failure or cardiac arrhythmias. This astute observation led to the establishment of the first coronary care unit in this country in 1962. Four years later, July 18, 1966, the Greenwich Hospital Association in Greenwich, Connecticut opened its coronary-intensive care unit

(CICU). It is the purpose of this report to review the management of patients with acute myocardial infarctions who were cared for in this unit.

Method

Patients suspected of having suffered acute myocardial infarctions were admitted to the CICU and placed on a cardiac monitor for a variable period of time ranging from one day to 38 days. An infusion of dextrose and water was started and continued for at least three days in all patients. Routine laboratory determinations including enzymes, electrocardiograms, blood counts and urines were done daily for at least three days. Other laboratory work included sedimentation rates, blood glucoses, blood urea nitrogens and serum cholesterol values. Hourly observations of the blood pressure, pulse rate and cardiac rhythm were made during the first 24 hours. Sixty percent (42) of the patients received anticoagulant therapy. Many received heparin intravenously followed by warfarin orally; the remainder, only warfarin orally. Digitalis was used in 60% (43) of the patients. Diuretics were used alone or in conjunction with digitalis therapy in 43% (30) of this series. Eighty-one percent (58) received antiarrhythmic drugs which included lidocaine, quinidine, procaine amide. Twelve patients received vasopressor drugs; and of these, 80% (10) died (Table 1). Other forms of therapy included

TABLE 1
FORMS OF THERAPY

	No. of Patients	% of Patients
Anticoagulants	42	60
Digitalis	43	60
Diuretics	30	43
Lidocaine	27	40
Procaine amide	7	10
Quinidine	26	39
Vasopressors	12	17

oxygen, analgesics, sedatives and so forth. A highly trained group of registered and licensed practical nurses rendered continuous nursing care to this

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group of patients. A medical resident physician was at close hand 24 hours a day. The CICU is a nine-bed unit with four beds monitored both at the bedside and remotely at the nurses' station using equipment which includes a memory tape, a system of alarms and a mobile cardioverter-defibrillator. In addition, the conventionally recommended equipment for this type of facility is available in the unit.

Results

During the period from July 18, 1966 to July 18, 1967, seventy-one patients were admitted to the CICU with clinical and laboratory evidence of acute myocardial infarction. This figure represented approximately one fresh infarction every five days. There were 50 men and 21 women in this group. The average age of the men was 62.6 years while that of the women was 70.3 years. The youngest patient was a 36-year-old man, and the oldest was a 91-year-old woman. The death rate for the year was 30% or 21 deaths, 16 of whom died while in the CICU and five of whom died after being discharged to other parts of the hospital (Table 2).

TABLE 2
MORTALITY

Sex	No. of Patients	Deaths in ICU	Deaths in Other Areas
Males	14	11	3
Females	7	5	2

The average patient stay in the CICU was six days, with a range of 40 minutes to 38 days. It is of interest that the month of April yielded the greatest number of patients suffering from acute myocardial infarctions (14), as well as the highest death rate (43%).

Forty-seven percent (34) patients had infarctions of the anterior wall while 46% (33) had posterior wall infarctions. Five percent (4) had subendocardial infarctions. Sixty percent (12) of the patients who died had posterior wall infarctions.

In the 21 patients who died of acute myocardial infarctions, there were three major causes of death. Fourteen died in cardiogenic shock, six died in intractable cardiac failure, and one died of a malignant arrhythmia (Table 3). Cardiogenic shock was the most serious complication and uniformly fatal in its fully developed form. It is characterized by a systolic blood pressure of 80 mm Hg or less, tachypnea, cyanosis, hypothermia, peripheral vascular constriction, severe oliguria, pulmonary con-

gestion and metabolic acidosis. A variety of therapeutic advances were used; all were unsuccessful. This substantially agrees with the experience of Cohn.⁴

TABLE 3
CAUSES OF DEATH

	No. of Patients	% of Patients
Cardiogenic shock	14	66
Intractable failure	6	29
Arrhythmia	1	5

Congestive heart failure was a very frequent complication in our series of patients. Sixty percent (43) of the patients showed evidence of congestive failure during the course of their infarctions. They developed this complication in the first 48 to 72 hours. Some patients showed mild pulmonary congestion on chest x-ray as the only evidence of cardiac failure. All the patients thought to be in heart failure were treated promptly with digitalis preparations and diuretics, regardless of the severity of heart failure. Thirty-seven of these responded well. The incidence of congestive failure in this series is not unlike that reported by Day,⁵ Lown,⁶ and Nachlas.⁷ Signs of congestive failure must be sought for early and repeatedly, for it is our impression that the early treatment of left ventricular failure prevents the subsequent development of other complications such as hypotension, shock, pulmonary emboli and arrhythmias. Furthermore, we agree with Lown⁶ and Askey⁸ that there is no contraindication to the use of digitalis in a fresh myocardial infarction.

Cardiac arrhythmias of all types were the most frequent complications observed in this group of patients. Eighty-two percent (58) had some form of cardiac arrhythmia observed, which is not unlike the 88% observed in Lown's series.^{6,7} Forty-seven percent (34) of the patients showed ventricular extrasystoles within the first four days of their illness, and most of these occurred in the first 48 hours. About one third of these patients developed ventricular tachycardia which required medication intravenously or DC cardioversion to terminate it. Since most of these cases will have ventricular extrasystoles occurring close to or on top of the preceding T-wave prior to the development of ventricular tachycardia, it is imperative that the early recognition and treatment of ventricular extrasystoles be aggressive, since one of the prime reasons for the establishment of the coronary care unit is

the prevention of malignant arrhythmias, a philosophy proposed by Lown.^{9,10} With this in mind, appropriate medications are administered at the earliest sign of potentially dangerous rhythm disturbances.

Ventricular fibrillation occurred in 13 of the 71 patients. Six of these had the "primary" type, and all were converted electrically to an effective rhythm. Four of these patients were discharged and are alive and well at present. The other two patients died of progressive myocardial failure. The remaining seven patients had "secondary" or terminal ventricular fibrillation as a consequence of irreversible cardiogenic shock. The latter form of ventricular fibrillation does not respond to treatment, whereas the "primary" variety can be converted electrically.

Various types of heart block were noted frequently in these patients. Ten patients exhibited evanescent, first-degree heart block and required no therapy. Twelve patients showed second-degree heart block, with and without bradycardia. Nine of these were treated using temporary, transvenous, demand-type pacemakers as described by Escher¹¹ and Furman.¹² One patient in the group with second-degree heart block developed repeated episodes of ventricular tachycardia which were poorly controlled pharmacologically and required electrical conversion on four occasions in a span of 18 hours. A transvenous pacemaker was implanted, and the patient was paced at a rate high enough to suppress his ectopic ventricular focus. After four days, the pacemaker was removed, and the patient recovered. Two patients in our group developed complete heart block and required permanent, asynchronous, transvenous pacemakers. Both are well after nearly one year.

Mural thrombosis and pulmonary embolism were two complications which were recorded infrequently. Three patients developed mural thrombi following myocardial infarction, and two of these died. One was found to have a peripheral arterial embolus. There was no evidence of embolism found in the other patient. Both of these patients were anticoagulated early. A third patient developed neurological symptoms after a through-and-through myocardial infarction. This patient was anticoagulated on the 11th day and made a complete recovery. Pulmonary emboli were detected in four patients despite early anticoagulation. Two survived (Table 4).

Discussion

The introduction of a CICU in our community

TABLE 4
COMPLICATIONS

	<i>No. of Patients</i>	<i>% of Patients</i>
Congestive failure	43	60
Arrhythmias (all types)	58	82
Ventricular tachycardia	10	14
Ventricular fibrillation	13	18
1° A-V block	10	14
2° A-V block	12	17
Complete heart block	2	2.8
Mural thrombi	3	4.2
Pulmonary emboli	4	5.5

hospital has resulted in a gratifying improvement in mortality statistics. It also brought to our attention some problems in the overall management of acute myocardial infarction which were not recognized heretofore. During the period of observation, approximately 120 patients were discharged with the primary discharge diagnosis of acute myocardial infarction. Only 60% of these patients received initial observation and care in the CICU. This indicates that the criteria for admission were either too rigid or the attending physicians were reluctant to admit their "good risk" patients to this area of the hospital. Certainly, the inclusion of these 50 "good risk" patients who were treated outside the CICU would have substantially lowered the 30% death rate in this group of patients so that it would more nearly approximate the national figure of 18% as quoted by Lown⁶ and Furman.¹² In this regard, Lown⁶ feels that one makes a mistake in attempting to have 100% accuracy in the diagnosis of acute myocardial infarction before admission to the coronary care unit takes place. He feels that a diagnostic accuracy of greater than 70% probably reflects delay of admission of some patients. In his initial group of patients, only 130 of 248 patients admitted to the coronary care unit proved to have a myocardial infarction. This is a diagnostic accuracy rate of 52%.⁶ We feel that the medical profession will come to appreciate the value of early observation in a coronary care unit of everyone suspected of having had a myocardial infarction.

The group of patients whose records we have analyzed represents a selected number of relatively "poor risk" patients suffering from acute myocardial infarction. We are, nevertheless, gratified with the results achieved. Certainly, many are alive and well today because of the treatment rendered in the CICU. In addition, we have learned much about the care of the patient suffering from acute myo-

cardial infarction, and our medical staff has come to appreciate the value of aggressive care of this group of patients. We expect to keep statistics so that more parameters can be reviewed periodically in the hope that we can treat this disease more effectively.

Acknowledgements

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References

1. Atherosclerosis: Fact Sheet, National Health Education Committee, Inc., New York, 1964.
2. *The Current Status of Intensive Coronary Care*—A symposium presented by The American College of Cardiology & Presbyterian-University of Pennsylvania Medical Center, New York: The Charles Press, 1966.
3. Meltzer, L. E.; Kitchell, J. B.: Incidence of Arrhythmias Associated with Acute Myocardial Infarction, *Progr Cardiovasc Dis* 9:50-63 (July) 1966.
4. Cohn, Jay N.: Myocardial Infarction Shock Revisited, *Amer Heart J* 74:1-3 (July) 1967.
5. Day, H. W.: Effectiveness of an Intensive Coronary Care Area, *Amer J Cardiol* 15:51-54 (Jan) 1965.
6. Lown, B., et al: The Coronary Care Unit, *JAMA* 199:188-198 (Jan) 1967.
7. Nachlas, M. M., et al: Continuous Monitoring of Patients With Acute Myocardial Infarction, *JAMA* 198:1-8 (Oct) 1966.
8. Askey, J. M.: Digitalis in Acute Myocardial Infarction, *JAMA* 146:1008-1010 (July) 1951.
9. Lown, B., et al: New Method for Terminating Cardiac Arrhythmias, *JAMA* 182:548 (Nov) 1962.
10. Lown, B., et al: Cardioversion of Ectopic Tachycardias, *Amer J Med Sci* 246:257 (Sept) 1963.
11. Escher, D. J.: The Present Status of Clinical Cardiac Pacing, *Amer Heart J* 74:126-132 (July) 1967.
12. Furman, S.: Cardiac Pacing, *Amer Heart J* 70:830-833 (Dec) 1965.

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Sex In The Sixth Grade

Experiences With Family Life Education For Sixth Grade Boys

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Since the Kinsey Report was published in 1948, there had been increased interest in and public discussion of sex and sexuality. By the middle 1950's, many schools had adopted family life education programs which tried to meet some of the needs which arose out of these concerns. Unfortunately, many of these deteriorated into social adjustment classes, poorly led and poorly organized efforts at group psychotherapy with students who treated the courses as a joke. As a result, most of these courses have been dropped from public school curricula.

However, these courses pointed out a general need for more information and more teaching of sex and sexuality in the schools, and this idea gradually has become accepted over the last decade. With the founding of Sex Information and Education Council of the United States, more information has been collected and more communities have become interested in sex education. It is generally assumed that young people need more information about sex and sexuality than they are receiving at home from their parents. As a result, many people feel that the school should step in and fill the gap. A major criticism of this has been the public's concern that morality be part of the curriculum. Most people accept the idea that sex is a difficult topic for parents and their children, and many are perfectly happy to permit the school to assume the responsibility, as is done in the Scandinavian countries. As a result, many school systems have adopted or are now in the process of developing fully coordinated programs of sex education to be used from kindergarten through grade 12. A major concern in devising these programs is the material to be included at each grade level.

My experience with a group of sixth grade boys may illustrate some of the information which these youngsters want at their particular time in life, so that programs may be based on classroom observations and the needs expressed by the students themselves.

During early January of 1967, the teachers and principal of a parochial school became aware of the fact that the boys in the sixth grade had discovered sex. The boys were whispering obscene remarks to the girls in their classes as well as passing obscene notes among themselves. When these notes fell into the hands of the teachers, the teachers became concerned and requested the help of a physician in organizing a program of sex and family life education for the boys in sixth grade.

The sixth grade girls had already had a discussion of menstruation and some films on menstrual hygiene with the school nurse. But until the time that this program was begun for the boys, no such arrangements had been considered necessary for them, a practice which is typical of much of the United States.

The Arrangements

A series of five sessions was programmed, consisting of three meetings with the school physician and two showings of motion pictures films about sexual growth and development. Meetings with the school physician were held every six weeks, and one film was shown approximately midway between each meeting with the doctor.

Each session with the school physician lasted two hours using question-and-answer format. In order to open up the discussion at the first meeting, the boys were asked to pass in written questions, and, from these, the first seminar was begun. Once these questions were fully answered, the boys had no further difficulty asking questions orally.

Topics

Of the first 23 questions submitted by the boys at the first meeting, six were about breasts. Obviously this was the most apparent change, the most noticeable sexual characteristic in their female classmates, and, therefore, the event which most interested and fascinated them. They wanted to know how the breasts develop as well as what makes them develop, and they expressed concern about their own burgeoning masculinity in questions about the possibility of men developing

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breasts as well. They expressed some confusion over the identity of pendulous flesh on fat men and breasts on women and were quite relieved to learn that men do not have breasts under normal circumstances.

After the topic of breasts was covered, the boys wanted to know more about masculine development. They asked about changing voice and the growth of beards. They wanted to know more about the appearance of body hair and the changes which occur in the genitalia. They were especially concerned about the timetable of events in the appearance of secondary sexual characteristics, some of the boys being quite immature at twelve whereas others were already well into puberty.

The presence of a set of fraternal twins in the class then raised questions about twinning and multiple births. The boys wanted to know how twinning happens, how there can be enough room for multiple babies in the mother's abdomen, and how the delivery is managed. Management of the delivery of twins then brought up the subject of management of the delivery of single babies, the management of breech births, and the use of medication for the mother during labor.

Having gotten the baby out of the mother's belly, they then wanted to know how the baby got in. Questions about intercourse, conception, and the events of and management of pregnancy came tumbling out in rapid succession. Since there were twenty-three boys in the class, several of the families had experienced miscarriages and the boys wanted to know about spontaneous abortions, and then about therapeutic and illegal abortions too.

The topic of abortions brought up the problems of diseases and drugs which affect the unborn baby and opened up the entire subject of venereal disease. The discussion of contagious diseases such as mumps and German measles then led to questions about sterility and factors which might affect the ability to have children or the ability to carry a pregnancy through to term.

Despite the fact the discussions were held in a Catholic parochial school, the boys were vitally concerned with contraception. They wanted to know the techniques which are available and the way in which each technique works. This then led into discussions of menstruation and egg production as well as a brief discussion on the manufacture of sperm.

As we gradually branched out from physical considerations, the boys wanted to know more about family relationships, dating, petting and marriage.

They wanted to know about divorce and divorce statistics, as well as why people get divorces. They wanted to know about the responsibilities of being a father as well as the responsibilities which go with being a husband.

All questions, whether written or verbal, were answered fully, openly, honestly and frankly. There was no attempt made to disguise information or to hide information in technical jargon. Simple, direct, everyday language was used, the only limitation being to avoid emotionally loaded four letter words.

The Results

The very first evidence of the effectiveness of the program was the abrupt spontaneous cessation of obscene remarks and the disappearance of the smutty notes from the school, despite the fact that nothing was said to the boys about the school's reasons for the program or the notes or remarks. Needless to say, the teachers and principal of the school were thoroughly enthusiastic about this particular result.

The parents of both the boys and the girls expressed great satisfaction. There were no objections from anyone, and in fact, great relief. The parents of the boys were relieved to have the subject broached and presented in an effective, unemotional manner. They were happy that the boys were receiving instruction which they felt inadequate to provide.

The parents of the girls were relieved that their daughters were no longer being subjected to the harrassment they had experienced earlier in the school year. Some of the parents of the girls even asked for a more thorough discussion for their daughters.

The boys too were pleased. They expressed satisfaction with the material and the way in which it was presented. And most encouraging, they were very disappointed when the series came to an end. I had the distinct feeling that if we could have continued for another three sessions of two hours each, I could have continued answering still more questions. However, at that point many of the questions were becoming repetitious, and we decided that the course had served its purpose.

Conclusions

The enthusiastic acceptance by the boys, their parents, the parents of the girls, and the school certainly indicates that programs such as this are needed in every school, in every community, and every state. The parents felt that once a subject

had been broached and once the basic information had been presented in a clear-cut factual manner they could continue the discussions at home. The hardest thing was getting started.

At least with sixth grade boys, the question-answer format seems to be an excellent way to handle sessions such as these. This technique meets the needs felt and expressed by the students and it allows the students to develop their own interests. Nevertheless, the program must be sufficiently long so as to be comprehensive. Undoubtedly much information which will be discussed will not be appreciated by 12 year old boys. Nevertheless, the fact that the information has been available will make it easier for them to go back and ask questions again later.

In general, the interest and the knowledge of 12 year old boys as well as their curiosity about sex and sexuality apparently has been seriously underestimated. Very few programs for sixth graders discuss all of the topics which the boys raised themselves. Yet these are the concerns and the interests and the thoughts of a group of alert 12 year olds who are already well into physiologic and psychological puberty.

The great concern with physical changes—breasts, beards and voice—reflects the narcissistic fascination a young adolescent's body has for him. Few are truly afraid of what is happening, unless of course they do not want to grow up. Then, every little change, every menstrual cycle, is a reminder of onrushing maturity. But most youngsters embrace adulthood gladly. Witness the rebellion against parental restraint which makes teenagers say, "They treat me like a child." The real fear is in the minds of parents and adults who worry what these young people will do with the information, afraid that narcissistic ego-centric teenagers will run right out and try it. In real life, discussions of this sort lead to decreased experimentation, not more.

Twelve year olds, especially boys, are not yet ready to approach feelings about sex. They rarely asked about feelings and when emotions were mentioned, they were uninterested. A more realistic time to discuss feelings is when boys are between 13 and 15.


The group size seemed effective. These boys were accustomed to working as a unit, and continued to do so. Altering the group or artificially controlling it would risk giving them the feeling that the adult leader was unsure of himself and needed to maintain a tight rein. The question-answer format was deliberately chosen because of this. Having worked with groups ranging in size from 12 to 75 members, I do not believe a group leader need be concerned with the size of the group—the important individual is the leader himself. If he is comfortable, the group will be too.

Should groups meet more often than once every three weeks? Probably. Weekly seems best. In this case, schedules required that meetings be arranged in the manner outlined, and, in comparison with other groups I have led, the sessions did not suffer because of the lapses.

Less comprehensive programs than the one developed with these sixth grade boys merely continue the poor practices of the past by sweeping sex under a patina of superficial attention. They salve the consciences of adults, but they effectively cut off communication with the youngsters.

Everyone, adults and young people alike, agree in the need for a program of sex and family life education in the elementary schools. Certainly it must be comprehensive and it must be presented in an open and honest manner without embarrassment and without an attempt to camouflage or hide information. Whether or not morality must also be a part of such programs is still open to debate. I personally do not believe that an oppressive presentation of adult morality is necessary. Most youngsters in America grow up in homes in which the standard of chastity is the ideal to which people aspire, although they don't necessarily practice it. Children grow up with the same aspirations and in general do not need to be reminded of it. What they need to understand is why morality has developed as it has, and why the adult world believes in chastity. For if they can develop their own answers and their own reasons for living chaste lives, that would be the ultimate success of a program in family life education for sixth grade boys.





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high under
the cuff.

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he forgets he has hypertension, gets hot
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For such
patients, consider

Regroton[®]

chlorthalidone 50 mg.
reserpine U.S.P. 0.25 mg.

To lower blood pressure
and allay anxiety in hypertension.

For brief summary of prescribing infor-
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chlorthalidone 50 mg.
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the once-a-day tablet for anxious hypertensives

Regroton is a combination of two basic antihypertensives designed to lower blood pressure and allay anxiety in hypertension. With Regroton he can keep his shirt on and you can keep his blood pressure down.

Before prescribing, please review carefully the indications, contraindications, warning, precautions, adverse reactions and dosage information below.

Regroton[®]
Each tablet contains:
chlorthalidone 50 mg.
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Indications: Hypertension.
Contraindications: History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.
Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs.
Use in pregnancy: Because chlorthalidone may cross the placental barrier and appear in cord blood and thiazides may appear in breast milk, this drug should be used with care in pregnant patients and nursing mothers. When used in women of childbearing age, the potential benefits of the drug should be weighed against the possible hazards to the fetus. Use of chlorthalidone may result in fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to

reserpine-treated mothers.
Precautions: Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, the drug should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Severe salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients.
Adverse Reactions: The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute

gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angitis are possible.
Average Dosage: One tablet daily with breakfast.
Availability: Pink, single-scored tablets in bottles of 100 and 1000. (B)46-600-C
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THE PRESIDENT'S PAGE

In November I spent some time at the New England Post Graduate Assembly. This is a most worthwhile meeting with practical and timely subjects. The whole meeting seems to be designed to enhance the knowledge of the busy practitioner. The program is arranged by New England physicians for New England physicians. This makes the Post Graduate Assembly a meaningful one for those who attend.

It is a most gratifying sight to see busy men, both recent graduates and those long out of school, sitting quietly, intent on what is being said. Most are busily taking notes for future digestion and reference. These men are in the room for one reason only, and they make sure they accomplish their purpose. Surely such assemblies are what keep medicine in this country the best in all the world.

We hear adverse criticism of medicine as a whole by those who know the least about it. This is probably no more than human nature. The childless couple seems to be able to point out all the errors in the way children are being reared. So it is and so it will always be. This is one important fact of each doctor's life which should be told as often as possible. There are few professions where continuing education is so important to the producer as well as the consumer. The doctor is not spending the time away from his practice and family for himself. By continuing his educational process, he makes himself more valuable to his patients and to his community. He feels a deep obligation to give his patients the best there is, and he is giving his time to make sure they get it.

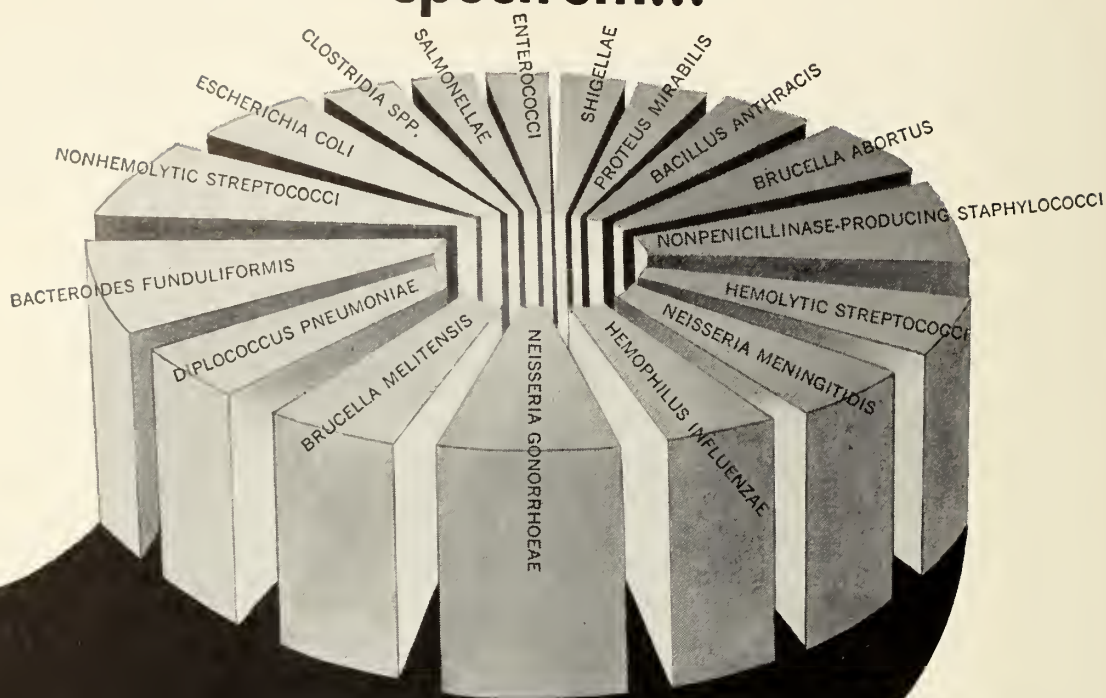
This article would never have been written if my wife had not chanced to have a conversation with a gentleman in the elevator at the hotel. This man had noted the large number of doctors in the hotel and wondered just what sort of a party they were having. This was her golden opportunity to impress a non-believer with the deep interest doctors have in self education. He shook his head in disbelief, but I can assure you, he was most impressed. And well he should be.

While I am on the subject, let me add that the Scientific part of our Annual Meeting is most worthwhile. I commend it to you. It is surprising how many of your old friends you will see there.

See you in Hartford in May.

NORMAN H. GARDNER, M.D.

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range of bacterial
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Indications: Infections due to susceptible strains of Gram-negative bacteria (including Shigellae, *S. typhosa* and other Salmonellae, *E. coli*, *H. influenzae*, *P. mirabilis*, *N. gonorrhoeae* and *N. meningitidis*) and Gram-positive bacteria (including streptococci, pneumococci and nonpenicillinase-producing staphylococci).

Contraindications: A history of allergic reactions to penicillins or cephalosporins and infections due to penicillinase-producing organisms.

Precautions. Typical penicillin-allergic reactions may occur, especially in hypersensitive patients. Mycotic or bacterial superinfections may occur. Experience in newborn and premature infants is limited and caution should be used in treatment, with frequent organ function evaluations. Safety for use in pregnancy is not established. In gonorrhoeal therapy, serologic tests for syphilis should be performed initially and

monthly for 4 months. Assess renal, hepatic and hematopoietic function intermittently during long-term therapy.

Adverse Reactions: Skin rash, pruritus, urticaria, nausea, vomiting, diarrhea and anaphylactic reactions. Mild transient elevations of SGOT or SGPT have been noted. Black tongue has been noted in some patients receiving the Chewable Tablets.

Usual Dosage: Adults—250 or 500 mg. q. 6 h. (according to infection site and offending organisms). Children—50-100 mg./Kg./day in 3 to 4 divided doses (depending on infection site

and offending organisms). Bacterial meningitis—150-200 mg./Kg./day in 6 to 8 divided doses. Children weighing more than 20 Kg. should be given an adult dose when prescribing orally. In parenteral administration, children weighing more than 40 Kg. should be given an adult dose. Beta-hemolytic streptococcal infections should be treated for at least 10 days.

Supplied: Capsules—250 mg. in bottles of 24 and 100. 500 mg. in bottles of 16 and 100. For Oral Suspension—125 mg./5 ml. in 60, 80 and 150 ml. bottles. 250 mg./5 ml. in 80 and 150 ml. bottles. Chewable Tablets—125 mg. in bottles of 40. Injectable—for I.M./I.V. use—vials of 125 mg., 250 mg., 500 mg., and 1 Gm. Pediatric Drops—100 mg./ml. in 20 ml. bottles.

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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1969 Annual Meeting of the House of Delegates will be held in the Terrace Room of the Hartford Hilton Hotel, Hartford. The first session of the House of Delegates will commence at 8:30 o'clock in the morning of Tuesday, May 13, with reference committee hearings at 11:45, followed by luncheon. The final session will commence at 8:30 o'clock in the morning of Wednesday, May 14.

Norman H. Gardner, President
Kenneth F. Brandon, Speaker of the House
Frederick C. Weber, Jr., Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates of December 11, 1968 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

Introduced by the Council

I.

ARTICLE VII—Panel on Physician-Hospital Mediation

Purpose: By adopting amendments to the Bylaws which established a Judicial Committee, May 1, 1968, the House of Delegates abolished the need for a "Panel on Physician-Hospital Mediation" since the functions of this panel have been transferred to the Judicial Committee. However, no corollary action was taken to delete the Panel from the Bylaws, and a further amendment is required as follows:

Amendment

ARTICLE VII—The Council

Section 1—Powers and Duties

Par. 12. Special Appointments. (*This paragraph, providing for the election of a Panel on*

Physician-Hospital Mediation and outlining its functions, shall be deleted in its entirety.)

II.

ARTICLE X—Council Committees, Subcommittees, Representatives and Advisors

Purpose: The proposal is made that, with respect to committees, representatives and advisors appointed or elected by the Council, it is neither necessary nor desirable for a listing of such committees, representatives and advisors and definitions of their functions to be made an integral part of the Bylaws. These appointments or elections are made by the Council, from time to time, either by request of an outside agency or on the initiative of the Council, and do not require confirmation by the House of Delegates. Further, when it is evident that one or more of these Council-

elected committees, representatives or advisors have served their purpose and are no longer needed, it should not be necessary to amend the Bylaws (with a 12 month delay) to dissolve or discharge them.

The Council should continue to have the authorization of the House of Delegates to appoint or elect these committees, representatives and advisors. This can be done by replacing the present specific provisions, which include names, functions, etc., with general provisions as outlined below:

Amendment

ARTICLE X—Committees of the Council

Section 1—Council Subcommittees (*Delete entire Section*).

Section 2—Standing Committees of the Council; Paragraphs 1-8 (*Delete entire Section*).

Section 3—Representatives and Advisors; Paragraphs 1-16 (*Delete entire Section*).

For the three deleted Sections, substitute the following:

ARTICLE X—Committees of the Council

Section 1—Standing Committees, Representatives and Advisors. The Council shall elect or appoint such standing committees, representatives and advisors as may, from time to time, be considered necessary or desirable. Any member of the Society in good standing may be elected or appointed to serve in these posts. The terms of members of standing committees, representatives and advisors shall be set by the Council, but, in any event, shall be reviewed annually by the Council. A current listing of such standing committees, representatives and advisors, including descriptions of the functions of each shall be maintained by the General Manager's office. In its discretion, the Council may dissolve or discharge these standing committees, representatives and advisors in the event that they are no longer necessary or desirable.

Section 2—Council Subcommittees. The Council may, from time to time, appoint ad hoc subcommittees to assist in expediting the business of the Council. Such ad hoc subcommittees shall be appointed from the membership of the Council and all appointments shall be reviewed annually by the Council at its first meet-

ing following the annual meeting of the House of Delegates. Upon completion of their assignments, such ad hoc subcommittees may be discharged by the Council at will.

Section 3* The Judicial Committee. The Judicial Committee shall consist . . . (as adopted by House of Delegates on 5/1/68).

* The election of Judicial Committee members is a "must" function of the Council; it is *not* optional.

III.

ARTICLE XI—Divisional Boards and Committees

Purpose: The Committee on Disaster Medical Care is currently listed under Article X—Committees of the Council under Section 3. Representatives and Advisors, but should have been listed under Standing Committees of the House of Delegates, which this amendment accomplishes.

Amendment

Section 3—Divisional Standing Committees

Par. G. Socio-Environmental Medicine Division
Add: Committee on Disaster Medical Care

Section 5—Duties of Standing Committees

Add new Paragraph 28:

The Council annually shall nominate to the House of Delegates a Committee on Disaster Medical Care, to consist of not less than six members and appoint the chairman thereof. The purposes of this committee shall be to study and keep informed on matters pertaining to the planning of programs designed to provide continuing medical care to the people of Connecticut under disaster conditions; and to cooperate with other agencies in the State engaged in similar activities.

IV.

ARTICLE VII, Section 3—General Manager

Purpose: The Council has approved changing the title of the General Manager to that of "Executive Director", it being found that the latter title is far more appropriate to professional association usage nationwide than is the former.

Amendment

The Council recommends that, in Article VII, Section 3—General Manager, and wherever else in the Bylaws the words "General Manager" appear,

these words be deleted and the words "Executive Director" be substituted therefor.

**SUMMARY OF ACTIONS
COUNCIL MEETING
Wednesday, January 15, 1969**

DELEGATES TO ANNUAL MEETING

The Bylaws of the Society provide that each county association is entitled to one delegate in the House of Delegates for each thirty-five Active or Life Members in the association or fraction thereof based on the membership as of December 31st of the immediately preceding year. According to this, the quota of delegates from each county association who should attend the Annual Meeting of the House of Delegates which will be held in Hartford, May 13, 14, 1969, and the Semi-Annual Meeting in December, 1969 is as follows:

<i>County</i>	<i>Membership Dec. 31, 1968</i>	<i>Official Delegates</i>
Fairfield	1001	29
Hartford	1151	33
Litchfield	147	5
Middlesex	120	4
New Haven	1028	30
New London	222	7
Tolland	29	1
Windham	71	3

**ELECTION OF COUNCILORS AND
ASSOCIATE COUNCILORS**

Councilors and Associate Councilors, who shall serve for two years, shall be elected this year at the annual meeting of each of the county associations in Hartford, Middlesex, New London and Windham counties. In accordance with the Bylaws, each component association having over 750 members may elect one additional Associate Councilor. Therefore, the Hartford County Medical Association should elect a Councilor and two Associate Councilors for a two year term.

No Councilor or Associate Councilor elected by a component association shall serve more than three successive terms of two years each in his respective office, but after a lapse of one term of two years, such Councilor or Associate Councilor shall be eligible for re-election.

Newly elected Councilors and Associate Councilors shall not assume office until after the Annual Meeting of the House of Delegates.

In the event that both the Councilor and the Associate Councilor(s) from a county association cannot be present, the President of the county association may appoint a substitute councilor.

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Grendon, Weber, Jr., Abbot, Fabro, Bradley, Rogol, Cramer, Farrell, Petrie, Spitz, Shepard, Nemoitin, Johnson, Friedberg, McDonald, Pelz, Granoff, Palomba and Roch.

Also present were: Mrs. Lindquist, Dr. Patterson, Dr. Hess, Mr. Donelan (AMA), Mr. Villano and Dr. Richards.

Absent were: Drs. Brandon, Egan, Purnell, J. M. Grant, R. F. Grant and Wilson.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the combined minutes of the meetings of November 13, 1968 and November 21, 1968.

Life Memberships

It was VOTED to approve application for Life Membership received from the following eligible Active Members:

Samuel M. Atkins, Waterbury (NHCMA)—1969
Walter J. Keefe, Cupertino, California (HCMA)—1969

C. F. Yeager, Easton (FCMA)—1969

Election of Student Member

It was VOTED to elect to Student Membership the following resident of Connecticut who is enrolled in a medical school in the United States:

Richard Dean Brodsky, 13 Cooper Road, West Haven

Washington Univ. School of Medicine—Class of 1972

Pre Med: Johns Hopkins University

Parent: Martin Brodsky

Date of Next Meeting

The Chairman announced that the next meeting of the Council will be held on Wednesday, February 5, 1969.

III. Old, New and Special Business

Replacements—Posts Held by Max Caplan, Deceased

Concerning a number of posts held by Dr. Caplan at the time of his death (December 1968), which do not require replacements being made at this time, it was VOTED to refer these matters to the Nominating Committee for 1969-70.

(Continued on page 194)

So he'll breathe easier: relieve anxiety while you relieve pain.

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Single-prescription, non-narcotic Equagesic may effectively relieve pain. *And* ease anxiety and tension.

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(meprobamate and ethoheptazine
citrate with aspirin)



IN BRIEF.

Contraindications: History of sensitivity or severe intolerance to aspirin, meprobamate or ethoheptazine citrate.

Warnings: *USE IN PREGNANCY:* Safety for use during pregnancy or lactation has not been established; therefore, it should be used in pregnant patients or women of child-bearing age only when the physician judges its use essential to the patient's welfare.

Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics—has resulted in dependence or habituation. Withdraw gradually after prolonged excessive dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance, with resultant slowed reactions and impaired judgment and coordination. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, patients should not operate machinery or drive. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously and in small amounts to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with gastric lavage and appropriate symptomatic therapy (CNS stimulants and pressor amines as indicated). Two instances of accidental or intentional significant overdosage with ethoheptazine and aspirin have been reported. These were accompanied by CNS depression (drowsiness and lightheadedness) but resulted in uneventful recovery. On basis of pharmacologic data, CNS stimulation could be anticipated, with nausea, vomiting and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]).

Adverse Reactions: Ethoheptazine and aspirin may cause nausea with or without vomiting and epigastric distress, in a small percentage of patients. Dizziness is rare at recommended dosage. Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses. Such patients may have had no previous contact with meprobamate and may or may not have an allergic history. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, discontinue meprobamate; do not reinstitute. Severe reactions, observed very rarely, include fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. These cases should be treated symptomatically including, when indicated, such medication as epinephrine, antihistamine and possibly hydrocortisone. A few cases of leukopenia, usually transient, have been reported on continuous use. Rarely, aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported, almost always in presence of known toxic agents.

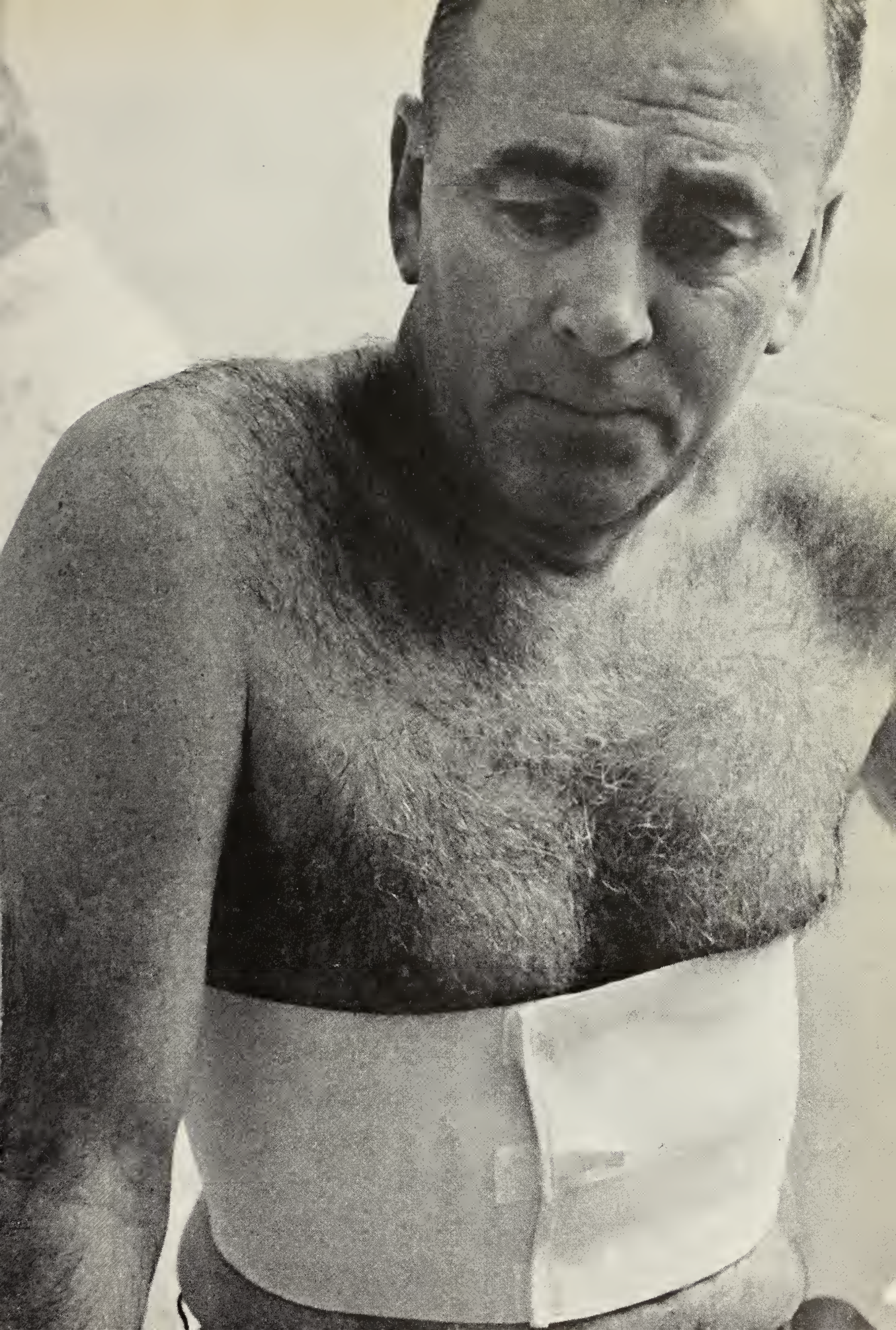
Overdosage: See precautions section for management of overdosage.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

Wyeth Laboratories Philadelphia, Pa.

Photo professionally posed.





Concerning posts for which immediate replacements are either necessary or desirable, actions were taken as follows:

- (a) *Delegate to AMA*: It was VOTED to appoint Michael A. Dean, Bridgeport, currently an Alternate AMA Delegate, to replace Dr. Caplan for the balance of the term 1/1/69-12/21/70. This interim appointment will require confirmation by the CSMS House of Delegates at the 1969 Annual Meeting.
- (b) *CSMS Vice-President*: It was VOTED to defer action on making this replacement, and to request the Board of Governors of the New Haven County Medical Association to submit an NHCMA nominee for this post in time for consideration at the meeting of February 5.
- (c) *CRMP Advisory Board*: It was VOTED to designate Frank K. Abbot, Waterbury, to replace Dr. Caplan as a CSMS-designated member of the Advisory Board of the Connecticut Regional Medical Program.
- (d) *Committee on Third Party Payments*: It was VOTED to appoint John R. Egan, Old Saybrook, to membership on this Committee as a replacement for Dr. Caplan.

Communication—Connecticut Medical Examining Board

Responding to a second request of the CMEB that notice of disciplinary action taken by the Board against an HCMA member be published in the Journal, the Council VOTED to publish *the fact* of the disciplinary action in the Journal, and to refer the entire question of such publication to the Judicial Committee for study and report.

Report—COMPAC Board of Directors

It was VOTED to receive as information a confidential report filed, at Council request, by the COMPAC Board of Directors. The report itemized the expenditures for COMPAC activities that had been charged against the CSMS Educational Grant to COMPAC made in 1968. It was further VOTED to forward a copy of the report to the Board of Directors of HCMA as information, the HCMA Board having originally asked the Council to request it.

Report—Liaison Committee with Welfare Commissioner

It was VOTED to accept, with commendation, a report filed by the chairman of the Liaison Committee, Kenneth F. Brandon, Hartford. In brief, the report covered various aspects of the organization of Medicaid (Title XIX) program administration and of the functions of the several committees and subcommittees advising the Welfare Depart-

ment on matters having to do with professional services (charges, utilization, etc.) rendered to Medicaid beneficiaries by Doctors of Medicine. The report indicates that further study is being made by the Medical Advisory Committee on some of the regulations contained in recently-issued Welfare Department Bulletin No. 2 to which quite a number of members of the Society have voiced strong objection (Example: Resolution introduced by the Executive Committee of LCMA at the last semi-annual meeting of the CSMS House of Delegates).

Treatise—Legal Relationship of Physician to Hospital

It was VOTED to receive as information, and with commendation, a treatise on the legal relationship of physicians to hospitals, prepared by J. Alfred Fabro, Torrington.

- (a) *Reports on CMS Century Contract vs. "Usual and Customary Charge" Concept; Liaison Committee with CG on Medicare B*: It was VOTED to accept a report filed by this Committee on its study and evaluation of the problems posed by the new, Insurance Commissioner-approved, CMS Century Contract to the furtherance of the "usual, customary and reasonable charge" concept of payment for physicians' services by third parties in Connecticut, both in the government-funded sector (Medicare, Medicaid, CHAMPUS) and in the private sector. It was further VOTED to approve two recommendations contained in the report: (1) That a survey by appropriate questionnaire be made among the membership of the Society to establish how many have signed, or intend to sign, Participating Physicians' Agreements in the Century Contract (CMS sets the figure at 60% or more of Connecticut practitioners); and (2) to undertake an immediate, intensive educational program among the membership, especially at the grass roots level, to familiarize all members as to the conflicting philosophies of "fee schedules" and "usual, customary and reasonable charges" as methods of third party payment for physicians' services and the hazards that the former pose to furtherance—or even continuation—of the latter. Also, that the County Association Councilors be requested to inform their respective governing bodies of the pressing importance of this matter and urge them to consider calling special membership meetings for the purpose of giving all interested members an opportunity to become fully apprised of the facts pertaining thereto. On recommendation (1), a

roll call vote revealed that all present voted "aye". On recommendation (2), a voice vote revealed that all present voted "aye" except for one abstention; i.e., there were no "nay" votes.

- (b) *Committee on Third Party Payments*: It was VOTED to receive as most helpful information, and with thanks, a report filed on the same subject by this Committee which contained recommendations for Council action which were similar in intent to those listed under (a) above.
- (c) *Miscellaneous Communications*: Received as information from several sources (individual members and groups of members) were communications which urged the Council to recognize the dangers to the "usual, customary and reasonable charge" concept posed by the CMS Century Contract and to take appropriate action to overcome or minimize such dangers.

Communication from Secretary of HEW

It was VOTED to receive as information a January 1st telegraphed message from HEW Secretary Wilbur J. Cohen (retiring) in which the Secretary announced that he was holding the Medicare B premium rate at \$8 (\$4 from enrollee; \$4 from Federal funds) for the next eighteen months, despite advice from SSS actuaries that the premium should be increased, and was appealing to all state medical societies to cooperate in getting physicians to hold their fees at present levels for at least 1½ years (until June 30, 1970). Not included in the telegram was mention of the directive (?regulation; ?suggestion) to insurance carriers administering Medicare B to keep allowable "reasonable" payments at present levels for the stipulated period no matter if claims indicate an increase in fees. Pursuant to receiving this information, the Council VOTED to request the President to appoint an ad hoc committee, with himself as chairman, to make communications contact with the incoming Secretary of HEW, probably in cooperation with the AMA, to present him with the opinions and policies of organized medicine regarding the proper relationships between government, insurance carriers, patients and physicians—this to be accomplished at an early date.

Legislative Matters

- (a) *Engagement of Legislative Agent*: On recommendation of the Chairman of the Committee on State Legislation, with the concurrence of

the Chairman of the Council, it was VOTED to authorize the engagement of Mr. Joseph P. Cooney, Hartford, as legislative agent for the Society for the biennium January 1, 1969-December 31, 1970, at an annual fee mutually satisfactory to Mr. Cooney and the Council.

- (b) *Bill on Alcoholism*: It was VOTED to approve, *in principle*, a bill which will be introduced at the 1969 General Assembly that defines alcoholism as a medical disease, rather than a civil offense, and calls for it to be treated medically rather than by imprisonment and/or fine. It was further VOTED to authorize John Donnelly, Chairman of the Committee on Mental Health, to speak for the Society in this regard. Some concern was expressed as to whether such definition could be used to grant immunity to alcoholics for crimes committed while under the influence, and it was agreed that a careful study of the bill should be made before the Society goes beyond approving it in principle.
- (c) *Bills on "Usual and Customary Charges"*: It was VOTED to have the Society sponsor two bills on this subject, one to permit extension of the usual and customary charge method of payment for physicians' services under Medicaid through the end of the current biennium, June 30, 1969 (the trial year ends March 1, 1969), and a second to provide for continuation of the payment method through the next biennium (1969-1971) and beyond.
- (d) *Bill on Immunity for Utilization Review Committees*: It was VOTED to reaffirm the Council's previous directive that the Society sponsor a bill which would provide immunity from civil suit for physicians serving on hospital utilization review committees without compensation. It was felt that the extent of the protection provided by liability insurance in Connecticut hospitals was unknown to the Council at this time, and, in any event, was probably not in effect in all hospitals throughout the State.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on January 15, 1969. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

OTOLARNGOLOGIST—Board eligible, will finish residency June 30. Military obligations complete, desires practice opportunity.

SURGEON—38 years old, Board certified, Connecticut license. Presently in military service, but desires to terminate active duty because of increasing administrative work and wish to be in direct care of patients. Available immediately.

PEDIATRICIAN—32 years of age, military obligations completed, Board eligible. Would like to join one or more pediatricians in any area of Connecticut. Available April 1, 1969.

Placement Opportunities

G.P.—Office space available with established physician, general medicine, spending half-time writing. Association and eventual partnership. Excellent schools and municipal facilities. Fairfield County.

PRACTICE FOR SALE—Well-established practice in Internal Medicine available. Modern offices and laboratory, large practice. New Haven County.

PSYCHIATRIST—Community-oriented mental hospital, to work in or direct a 500-bed comprehensive mental health center, one of several units in 1600-bed hospital. Opportunity for teaching, clinical work and research, also to work with or direct a team of social workers, psychiatric residents, psychologists, occupational therapists and approximately 190 nursing staff personnel. Opportunity for association with Wesleyan University, Yale and UConn. Qualified candidates may be considered for other senior staff positions. Liberal benefits with housing available at a nominal charge, annual leave to attend medical conventions. Send all particulars in first letter, including references to Mehadin K. Arafah, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

EDUCATIONAL OPPORTUNITY—PSYCHIATRIC RESIDENCIES available in a community oriented mental hospital. Comprehensive treatment facility for central Connecticut. Associated with Yale Departments of Psychiatry and Neurology which provides supervision and opportunities for training in areas of special interest. Special arrangements can be made for residents to be accepted for degrees in community mental health

and hospital administration at the Yale School of Epidemiology and Public Health. Personal analysis can be easily arranged. Many fringe benefits. Send all particulars in first letter to Mehadin K. Arafah, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

EDUCATIONAL OPPORTUNITY—GENERAL PRACTITIONER to specialize in psychiatry. For psychiatric residency available in community-oriented mental hospital associated with Yale, which provides clinical demonstrations, teaching and supervision in hospital. Opportunities for training in areas of special interest. Psychoanalytic training available at Western New England Psychoanalytic Institute. Liberal fringe benefits. Send all particulars in first letter to Mehadin K. Arafah, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

EDUCATIONAL OPPORTUNITY—Investigate Rehabilitation Medicine. Young speciality with wide opportunities in teaching, research and clinical care of increasing number of physically handicapped. Rehabilitation specialists diagnose and manage disorders of function, primarily chronic disorders of neuro-musculoskeletal system such as amputees, paraplegia, arthritis, strokes and cerebral palsy. In addition to using conventional medical or surgical treatment, rehabilitation management aims to develop each patient's residual abilities to optimal levels through prescription of appropriate combination of medical and physical therapy, mechanical devices, practical self-care and occupational skills, vocational training, psychological support and social readjustment. For information, write: Robert C. Darling, M.D., Chairman, Department of Rehabilitation Medicine, College of Physicians & Surgeons, 630 West 168th St., New York, N.Y. 10032.

Physician Reprimanded by Examining Board

Notice has been received from the Connecticut Medical Examining Board that the Board has formally reprimanded Raymond S. Keefe, M.D., Hartford, for not having been sufficiently "conscientious and ethical" in the matter of appropriately examining patients before treating or prescribing medications for them, and for not keeping proper patient records regarding prescribed drugs.

This notice is published at the request of the Connecticut Medical Examining Board. The notice is dated June 6, 1968.

Extrapyramidal Side Effects of Psychotropic Drugs

David J. Greenblatt, Richard I. Shader, M.D.
and Alberto DiMascio, Ph.D.

Some of the most bizarre and disturbing side effects of psychoactive drugs involve the extrapyramidal motor system. A high proportion of patients receiving this kind of medication experience one or a number of characteristic disorders of motor function and posturing, which are collectively classified as extrapyramidal symptoms (EPS).

Historically, the phenothiazine tranquilizers, or neuroleptics, are the agents with which EPS have been most often associated. Recently, however, newer classes of drugs, the butyrophenones and thioxanthenes, have also been noted to produce EPS. The majority of investigators cite overall incidence figures showing that more than 15 per cent of patients treated with phenothiazine drugs experience some type of EPS. The butyrophenones, of which haloperidol (Haldol) is the prototype, produce EPS at a rate similar to the phenothiazines, while the thioxanthenes, exemplified by chlorprothixene (Taractan), induce a significantly lower incidence of these symptoms.

Although the incidence and severity of EPS vary with class of drug, milligram potency of the specific drug used, dosage level, and length of the treatment period, it is not known what actually determines a given individual's susceptibility to the development of EPS.¹⁻³ Each patient seems to have his own dose as well as drug susceptibility level. Thus some fail to develop EPS after receiving high doses of potent neuroleptics over long periods of time, while others experience severe and

disabling symptoms after the first dose or at very low doses.

The majority of phenothiazine-induced extrapyramidal disorders are entirely reversible in nature, and disappear soon after discontinuation or lowering of drug dosage. These reversible disorders fall into three broad categories (Table 1).⁴⁻⁷

TABLE 1

DESCRIPTION OF REVERSIBLE EXTRAPYRAMIDAL SYMPTOMS

A. <i>Dystonic Reactions</i>
1. <i>Dystonias</i>
Exaggerated Posturing of Head, Neck or Jaw: Neck Twisting, Torticollis
Spasms of Muscles of Lips, Tongue, Face or Throat; Tongue Protrusion or Curling, Facial Grimaces and Distortions, Difficulty in Speech and Swallowing
Hyperextension of Neck and Trunk: Opisthotonus (arching of back)
Oculogyric Crisis (Fixed Upward Gaze)
2. <i>Dyskinesias</i>
Clonic Involuntary Contractions of Muscle Groups: Facial Tics and Twitches, Chewing Movements, Lip Smacking, Blinking, Aimless Movements of Tongue, Shoulder Shrugging, Pedaling Movements of Legs
B. <i>Akathisia</i>
Inability to Sit Still or Sleep
Intolerance of Inactivity
Continuous Agitation and Restless Movement
Rocking and Shifting of Weight While Standing
Shifting of Legs and Tapping of Feet While Sitting
C. <i>Parkinsonian Reactions</i>
1. <i>Akinesia</i>
Rigidity and Immobility
Stiffness and Slowness of Voluntary Movement
Mask-like Immobility of Facies
Stooped Posture
Shuffling, Festinating Gait
Slow, Monotonous Speech
2. <i>Tremor</i>
Regular Rhythmic Oscillations of Extremities, Especially Hands and Fingers
Pill-Rolling Movements of Fingers

The *dystonic reactions*, although occurring less frequently than the other two classes of disorders, are dramatic in appearance and are usually mani-

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ALBERTO DIMASCIO, Ph.D., Research Associate in Psychiatry, Harvard Medical School; and Co-Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center.

fest within the first few days of drug therapy. The symptoms appear and disappear intermittently and spontaneously, lasting from a few minutes to several hours. The dystonic reactions occur most often in children, adolescents, and young adults, with males predominating over females in incidence, and are usually induced by the piperazine class of phenothiazines,⁶ or by the butyrophenones. These reactions can be separated into the *dystonias*, which are prolonged abnormal tonic contractions of muscle groups, especially about the head and neck, resulting in odd posturing and strange facial expressions; and the *dyskinesias*, consisting of tics, spasms and other clonic types of muscular contractions.

Akathisia, or motor restlessness, is characterized by an appearance of continuous agitation. This syndrome occurs at any time from days to months following onset of drug therapy, and tends to appear and disappear spontaneously. Patients of middle age are most susceptible to development of akathisia, with females predominating over males in frequency.

The *parkinsonian reactions* are so named because of their clinical similarity to the symptoms of both the idiopathic familial and the postencephalitic forms of true parkinsonism.⁸ The reactions occur most frequently in the geriatric group of patients, with females predominating over males. The symptoms tend to be continuous in nature, are manifest within the first few months of drug therapy, and are most often induced by the dimethylaminopropyl group of phenothiazines,⁶ of which chlorpromazine (Thorazine) is the prototype. The parkinsonian reactions are roughly divided into *akinesia*, characterized by rigidity, immobility, and reduction of voluntary activity, and *tremor*, of which the regular, rhythmic 4-8 per second oscillation of the hands and fingers is the most familiar.

Alleviation of extrapyramidal symptoms usually can be achieved by discontinuation or dosage reduction of the psychotropic medication. However, since this procedure also results in some degree of sacrifice of the anti-psychotic benefits of the drug, the usual method of combating drug-induced EPS consists of simultaneous therapy with any of a number of synthetic antispasmodic parasympatholytic agents. Trihexylphenidyl (Artane), benzotropine (Cogentin), and biperidin (Akineton) in the past have been the most popular of these agents. Recently procyclidine (Kemadrin) and parenterally-administered diphenhydramine (Benadryl) have come into wide use. These "antiparkinsonian"

drugs are of some value in alleviating dystonias and the rigidity of the parkinsonian reaction, and do not diminish the psychotropic value of the phenothiazine therapy.⁷ But although drug-induced EPS respond somewhat more favorably to antispasmodic medication than do the symptoms of true parkinsonism, most patients will still experience only partial relief of phenothiazine-induced side effects, with some patients finding no relief at all. The antispasmodics often fail to produce remission of the symptoms of dyskinesia, akathisia, and the parkinsonian tremor, and in themselves can produce atropine-like CNS toxicity, together with peripheral anticholinergic side effects such as dryness of the mouth, blurring of vision, and paralysis of visual accommodation.⁹ The physician employing antiparkinsonian medication for the relief of either drug-induced EPS, or the symptoms of true parkinsonism, must titrate the patient's drug dose to the proper level, and then be prepared to adjust dosages and shift drugs as it becomes necessary.⁹

In contrast to the reversible extrapyramidal disorders, the more rare *persistent* or *tardive dyskinesias*,¹⁰⁻¹³ (Table 2) occur very late in the course

TABLE 2
DESCRIPTION OF THE TARDIVE DYSKINESIAS

Lingual-facial hyperkinesias: smacking and licking of the lips, sucking movements, chewing movements, rolling and protrusion of the tongue, blinking, grotesque grimaces and spastic facial distortions.
Choreo-athetoid movements of extremities: clonic jerking of fingers, ankles, and toes.
Tonic contractions of neck and back muscles.

of drug treatment, usually more than six months after the onset of therapy. The tardive dyskinesias are characterized by grotesque hyperkinetic activity in the oral region, and are usually seen in chronic deteriorating schizophrenics in the 50-75 year age group, with females somewhat more susceptible than males. Many patients afflicted with this syndrome also demonstrate evidence of organic brain disease, resulting from any of a number of causes.

Manifestations of tardive dyskinesia may begin late during the course of phenothiazine therapy, or may occur following a lowering of dosage or discontinuation of the drug. Symptoms tend to persist for many months or years after the termination of therapy, perhaps for the duration of the patient's life. The tardive dyskinesias do not respond at all to antiparkinsonian medication; occasionally the syndrome is actually made worse by this type of drug.¹² Alleviation of symptoms can be achieved

only by reinstating high doses of phenothiazines, or by the administration of sleep-producing doses of sedative-hypnotics. Fortunately, as is uncharacteristic of the true choreas, drug-induced dyskinetic movements tend to disappear during sleep.¹⁰

The pressing need for more effective methods of treating both naturally-occurring and drug-induced extrapyramidal disorders has stimulated considerable biochemical research in this field. Dopamine, the biosynthetic precursor of norepinephrine, has received much attention in this connection. Relatively high concentrations of dopamine are known to exist in the central nervous system, especially in the basal ganglia and substantia nigra;¹⁴ it is postulated that dopamine may serve as a synaptic transmitter substance in these areas.

In naturally-occurring Parkinson's disease, the major neuropathological correlate involves these very areas of the brain. There is shrinkage and neuron loss in the basal ganglia, and depigmentation of the melanin-containing cells of the substantia nigra.^{15, 16} Biochemically, a marked reduction in the dopamine content of these areas has been demonstrated by some authors in autopsy studies.^{14, 17} Moreover, parkinsonian patients also excrete abnormally small amounts of dopamine and its major metabolite, homovanillic acid (HVA).^{17, 18} From these facts comes the hypothesis that a dopamine deficiency in the basal ganglia and substantia nigra, leading to an understimulation of dopamine receptors in these areas, is the physiological defect in Parkinson's disease.¹⁸ In idiopathic familial parkinsonism, an inborn error of metabolism, involving a possible deficiency of the enzyme DOPA decarboxylase,¹⁷ may be the cause of the defect, while in post-encephalitic parkinsonism, the biochemical damage is probably acquired secondary to the inflammatory process.⁸

Drug-induced EPS presumably also involve an interaction with dopamine metabolism. It is known that phenothiazines do not inhibit the activity of enzymes in the dopamine biosynthetic pathway,¹⁹ thus, it is unlikely that a decreased synthesis of dopamine is the mechanism of drug-induced EPS. However, chlorpromazine and related compounds are known to have peripheral alpha-adrenergic blocking properties, and it seems plausible that these drugs also block dopamine receptors in the central nervous system.^{14, 19, 20} This hypothesis is supported by the observation that rats given high doses of phenothiazines show no changes in basal ganglia dopamine levels, but show elevated HVA concentrations in this area;¹⁹ this is consistent with

a possible dopamine receptor blockade in which an increased turnover of dopamine results from an interference with the feedback inhibition of synthesis. Moreover, it has been reported that humans treated with phenothiazines show increased urinary HVA levels at the same time as their extrapyramidal symptoms are most severe.²¹

The concept of the phenothiazines as blockers of CNS dopamine receptors has further implications involving mechanisms of psychosis. It is known that toxic doses of amphetamines can produce auditory and visual hallucinations, paranoid thinking, and looseness of logical associations in speech, all of which are characteristic of a schizophrenic reaction.²² It is also known that a single dose of chlorpromazine can dramatically relieve the symptoms of amphetamine poisoning.²³ If chlorpromazine acts as a blocker of dopamine receptors, then amphetamine psychosis is probably caused by interaction with dopamine receptors;¹⁴ in view of the structural similarity between dopamine and amphetamine, this is one, but by no means the only,²⁴ reasonable speculation as to the mechanism of amphetamine psychosis. Further, it has been hypothesized that schizophrenia itself somehow results from an overstimulation of dopamine receptors throughout the CNS.¹⁴ The antipsychotic activity of phenothiazines results from a dopamine-receptor blockade, with extrapyramidal side effects resulting from such a blockade in the basal ganglia and substantia nigra.^{14, 19, 20}

An implication of this hypothesis is that the antipsychotic activity of the phenothiazines must somehow be paralleled by the development of EPS.¹⁴ Many foreign investigators do indeed believe that these effects are inseparable.^{25, 26} Most American researchers, however, conclude that EPS need not accompany antipsychotic activity.⁷ This conclusion is substantiated by the observation that anti-parkinsonian drugs may relieve EPS but not diminish the psychotropic effect of phenothiazines. Moreover thioridazine (Mellaril), a piperidyl phenothiazine, is as effective in antipsychotic activity as the related drugs, but causes a much smaller incidence of EPS.²⁷ Our proposed mechanism for the antipsychotic action of phenothiazines would clearly require modification to explain these facts.

The hypothesis that parkinsonism results from an understimulation of dopamine receptors in the basal ganglia and substantia nigra, due either to diminished dopamine synthesis in the familial disease, or due to receptor blockade in the drug-induced syndrome, implies that dopamine or related

compounds may have a place in the treatment of these disorders. Recent studies¹⁸ using L-DOPA, the biosynthetic precursor of dopamine, indicate that large oral doses of this compound, in the range of 8 gm. per day, can produce dramatic relief of the rigidity of Parkinson's disease, presumably by increasing the dopamine content of the extrapyramidal centers. Other less extensive studies show that similar relief can be obtained from drug-induced EPS.²⁸ Although these treatments are still largely in the experimental stage, the use of L-DOPA holds promise for the alleviation of extrapyramidal disorders.

Combined treatment with major tranquilizers and antidepressant drugs, although probably of no special therapeutic value,²⁹ has been claimed to reduce the extrapyramidal side effects associated with the phenothiazine alone.^{30, 31} However, a survey of the literature reveals a paucity of studies in which this claim has been properly documented. In one double blind study,³² the combination of chlorpromazine and imipramine produced fewer adverse neurological side effects than the chlorpromazine-placebo combination; the numerical difference was small and not statistically significant. Further properly controlled studies will probably reveal that the adjunct of antidepressants to phenothiazine therapy has little or no effect upon the incidence of EPS.

Antidepressant drugs alone do not block dopamine receptors or inhibit the synthesis of dopamine.¹⁴ However, a persistent fine tremor in the upper extremities, different than the tremor induced by phenothiazines, has been reported in up to 10% of patients receiving tricyclic antidepressants.³² This tremor is unrelieved by antiparkinsonian medication. There is no obvious physiological model to explain this phenomenon. Similarly, although amphetamine drugs are postulated to stimulate, rather than block, dopamine receptors, a recent report³⁴ describes four patients treated with therapeutic doses of d-amphetamine who developed dystonias of the head and neck, ticklike dyskinesias in the oral region, and choreo-athetoid movements of the hands. These disorders were similar to the phenothiazine-induced EPS, and were not mere extensions of the usual pharmacologic effects of the amphetamines.

These observations show that EPS can occur as side effects of drugs other than phenothiazines, and demonstrate the inadequacy of our knowledge of the mechanisms of drug interactions with the CNS.

The alert physician will realize that in disease

states in which muscular tone is affected, the response to phenothiazines may be considerably altered. Recent clinical observations indicate that patients with hypoparathyroidism may be especially susceptible to the development of EPS following phenothiazine administration. In one report³⁵ a series of untreated hypoparathyroid patients were challenged with small doses of prochlorperazine; all of these patients experienced severe dystonic reactions within 36 hours of drug administration. Normally, the dystonic reactions are the least common of the phenothiazine-induced extrapyramidal effects.¹ Thus a physician who observes a severe dystonic reaction shortly after a small initial dose of a phenothiazine should suspect hypoparathyroidism in that patient. Other such reports of altered responses to phenothiazines in disease states will likely occur in the future.

References

1. Ayd, F. J.: A Survey of Drug-Induced Extrapyramidal Reactions. *J.A.M.A.* 175: 1054-1060, 1961.
2. Ayd, F. J.: Neuroleptics and Extrapyramidal Reactions in Psychiatric Patients. *Revue Canadienne de Biologie* 20: 451-459, 1961.
3. Schiele, B. C.: Symposium on Side Effects and Drug Toxicity. *Psychopharmacology Bulletin* 4: 56-61, 1967.
4. Schmidt, W. R., and Jarcho, L. W.: Persistent Dyskinesias Following Phenothiazine Therapy. *Archives of Neurology* 14: 369-377, 1966.
5. Sheppard, C., and Merlis, S.: Drug-Induced Extrapyramidal Symptoms: Their Incidence and Treatment. *American Journal of Psychiatry* 123: 886-889, 1968.
6. *New Drugs Evaluated by the A.M.A. Council on Drugs*. Chicago: American Medical Association, 1967.
7. Chien, C. P., and DiMascio, A.: Drug-Induced Extrapyramidal Symptoms and Their Relations to Clinical Efficacy. *American Journal of Psychiatry* 123: 1490-1498, 1967.
8. Harrison, T. R. et al (eds): *Principles of Internal Medicine*, 5th Edition. New York: McGraw-Hill, 1966.
9. Friend, D. G.: Anti-Parkinsonism Drug Therapy. *Clinical Pharmacology and Therapeutics* 4: 815-822, 1963.
10. Degkwitz, R., and Wenzel, W.: Persistent Extrapyramidal Side Effects After Long-Term Application of Neuroleptics. In *Neuropsychopharmacology*. Brill, H. (ed.) The Hague, Netherlands: Excerpta Medica Foundation, 1967, p. 608-615.
11. Kline, N. S.: On the Rarity of "Irreversible" Oral Dyskinesias Following Phenothiazines. *American Journal of Psychiatry* 124 Supplement: 48-54, 1968.
12. Crane, G. E.: Tardive Dyskinesia in Patients Treated with Major Neuroleptics: A Review of the Literature. *American Journal of Psychiatry* 124 Supplement: 40-48, 1968.
13. Greenblatt, D. L., Dominick, J. R., Stotsky, B. A., and DiMascio, A.: Phenothiazine-Induced Dyskinesia in Nursing-Home Patients. *Journal of the American Geriatric Society* 10: 27-34, 1968.
14. Van Rossum, J. M.: The Significance of Dopamine-Receptor Blockade for the Action of Neuroleptic Drugs. In *Neuropsychopharmacology*. Brill, H. (ed.) The Hague, Netherlands: Excerpta Medica Foundation, 1967, p. 321-329.

15. Anderson, W. A. D.: *Synopsis of Pathology*, 6th Edition. St. Louis: C. V. Mosby, 1964.
16. Adams, R. D., and Sidman, R. L.: *Introduction to Neuropathology*. New York: McGraw-Hill, 1968.
17. Symposium on Adverse Reactions to Psychotropic Drugs. *Psychopharmacology Service Center Bulletin* 3: 3-23, 1965.
18. Cotzias, G. C., Papavasiliou, P. S., Gellene, R., and Aronson, R. B.: Parkinsonism and Dopa. *Transactions of the Proceedings of the Association of American Physicians*, (In Press).
19. Pletscher, A.: Pharmacologic and Biochemical Bases of Some Somatic Side Effects of Psychotropic Drugs. In *Neuropsychopharmacology*. Brill, H. (ed.) The Hague Netherlands: Excerpta Medica Foundation, 1967, p. 571-577.
20. Pletscher, A., and DaPrada, M.: Mechanism of Action of Neuroleptics in *Neuropsychopharmacology*. Brill, H. (ed.) The Hague, Netherlands: Excerpta Medica Foundation, 1967, p. 304-311.
21. Bruno, A., and Allegranza, A.: The Effect of Haloperidol on the Urinary Excretion of Dopamine, Homovanillic and Vanilmandelic Acids in Schizophrenics. *Psychopharmacologia (Berlin)* 8: 60-66, 1965.
22. Connell, P. H.: *Amphetamine Psychosis*. London: Chapman and Hall, 1957.
23. Espelin, D. E., and Done, A. K.: Amphetamine Poisoning: Effectiveness of Chlorpromazine. *New England Journal of Medicine* 278: 1361-1365, 1968.
24. Hanson, L. C. F.: Evidence that the Central Action of (+)—Amphetamine is Mediated Via Catecholamines. *Psychopharmacologia (Berlin)* 10: 289-297, 1967.
25. Delay, J., and Deniker, P.: Apport de la Clinique à la Connaissance de l'Action des Neuroleptiques. In *Extrapyramidal System and Neuroleptics*. Bordeleau, J. (ed.) Montreal: Editions Psychiatriques, 1961.
26. Haase, H. J.: Extrapyramidal Modification of Five Movements—A "Condition Sine Qua Non" of Fundamental Therapeutic Action of Neuroleptic Drugs. *Revue Canadienne de Biologie* 20: 425-449, 1961.
27. Grinspoon, L., Shader, R. I., Chatterjee, S., and Cohler, J.: Side Effects and Double-Blind Studies: I. A Clinical Comparison Between Thioridazine Hydrochloride and a Combination of Phenobarbital and Atropine Sulfate. *Journal of Psychiatric Research* 2: 247-256, 1964.
28. Bruno, A., and Bruno, S. C.: Effects of L-DOPA on Pharmacological Parkinsonism. *Acta Psychiatrica Scandinavica* 42: 264-271, 1966.
29. Freeman, H.: The Therapeutic Value of Combinations of Psychotropic Drugs: A Review. *Psychopharmacology Bulletin* 4: 1-27, 1967.
30. Hedberg, D. L., and Glueck, B. C.: Drug Combinations in Schizophrenia. In *Neuropsychopharmacology*. Brill, H. (ed.) The Hague, Netherlands: Excerpta Media Foundation, 1967, p. 496-499.
31. Delgado, J. N., Cosgrove, F. P., and Isaacson, E. I.: Certain Antidepressant Agents Found to Cause Various Adverse Reactions. *Texas Medicine* 63: 104-109, 1967.
32. Kurland, A. A., Bethou, G. D., Michaux, M. H., and Agallianos, D. D.: Chlorpromazine-Chlordiazepoxide and Chlorpromazine-Imipramine Treatment: Side Effects and Clinical Laboratory Findings. *Journal of New Drugs* 6: 80-95, 1966.
33. Klerman, G. L. and Paykel, E. S.: The Tricyclic Antidepressants. In *Principles of Psychopharmacology*. Clark, W. G., et al (eds.) New York: Academic Press, 1968. (In Press)
34. Mattson, R. H., and Calverley, J. R.: Dextroamphetamine-Sulfate-Induced Dyskinesias. *J.A.M.A.* 204: 400-402, 1968.
35. Schaaf, M., and Payne, C. A.: Dystonic Reactions to Prochlorperazine in Hypoparathyroidism. *New England Journal of Medicine* 275: 991-995, 1966.

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Electrocardiograms of the Month

Montefiore Hospital and Medical Center
The Bronx, New York

Editors

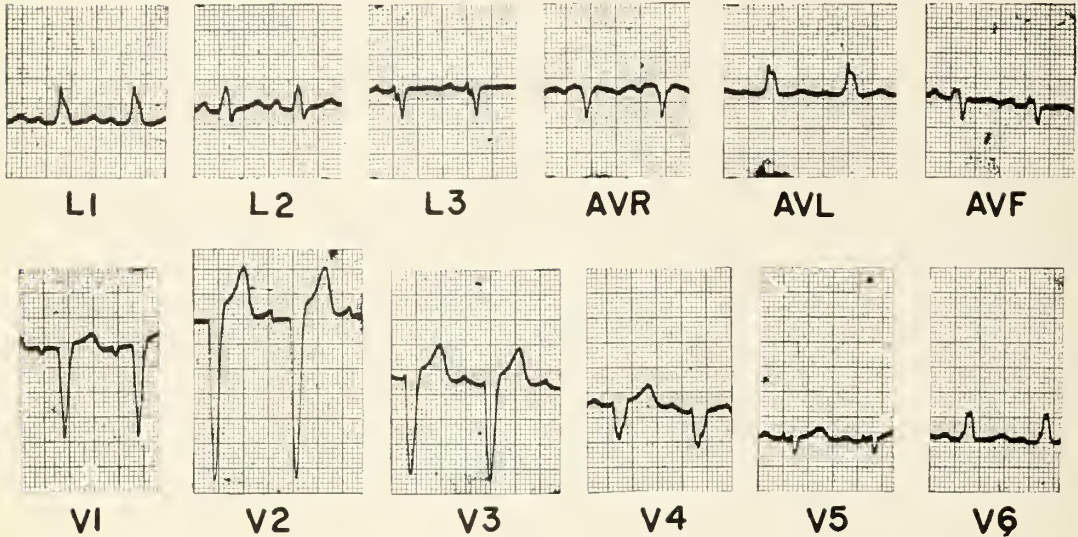
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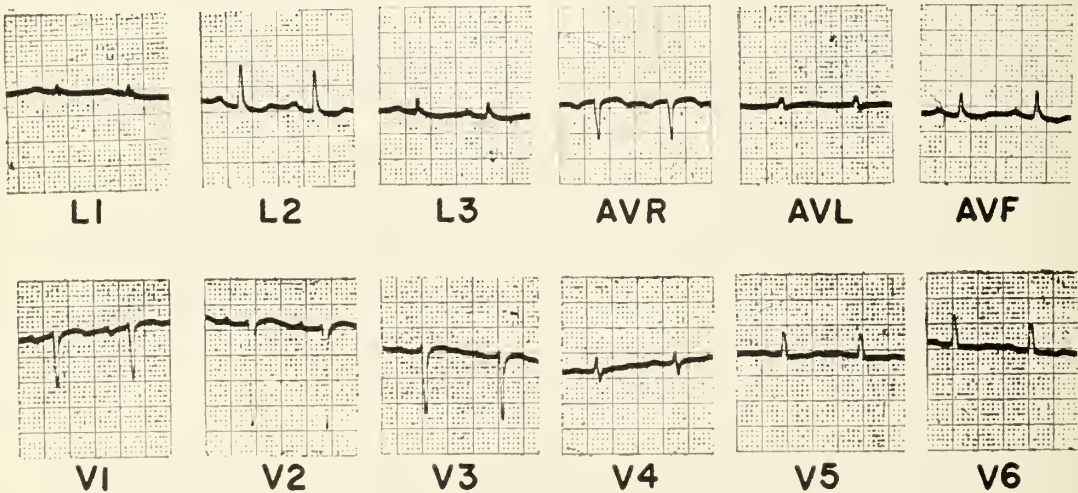
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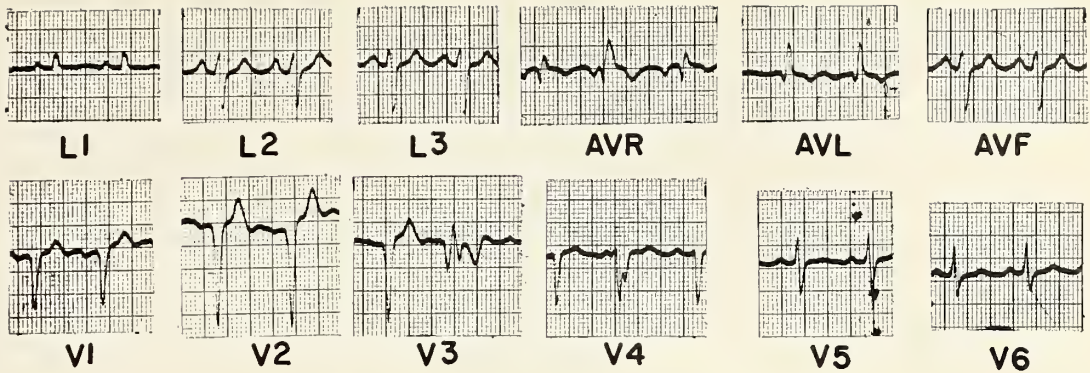
10/9/65



QUESTION 5. Two electrocardiograms were performed on a thirty-year-old woman fourteen months apart. What is the interpretation of the electrocardiograms, and what are the possible clinical diagnoses?

12/17/66





QUESTION 6. This tracing was obtained on a forty-five-year-old man with a history of previous myocardial infarct. What is the interpretation?

Electrocardiograms of Month

ELUCIDATION

QUESTION 5. The electrocardiogram dated 10/9/65 shows regular sinus rhythm at a rate of 95 per minute. The QRS complexes are widened to 0.14 seconds. The Q wave is absent in leads I, aVI, V₅, and V₆, with a delayed R wave. The T wave, however, is upright in these leads. These changes represent a ventricular conduction delay of the left bundle branch block type. The electrocardiogram of 12/17/66 has a normal contour with a QRS of 0.06 seconds. There is no delayed R wave in leads I, aVI, V₅, and V₆, although a Q wave is not present in these leads. The conduction is now normal. The only abnormalities are the nonspecific T-wave changes in leads I, II, aVf, V₄, V₅, and V₆.

The presence of and the disappearance of left bundle branch block in a thirty-year-old woman is unusual. Drug toxicity from quinidine or procaine amide might produce left bundle branch block. Occasionally left bundle branch block may occur transiently during a bout of tachycardia. Left bundle branch block in this patient was due

to myocarditis. Following a period of from seven to eight months of bed rest, the patient was improved clinically. The electrocardiogram reflects this improvement.

QUESTION 6. The tracing shows regular sinus rhythm and left axis deviation of a pathologic degree, greater than minus 30 degrees. There are ventricular premature contractions in aVr, V₃, and V₄. There is a QS pattern in V₁, V₂, and V₃, with a small initial R wave in V₄. A small Q wave is present in lead aVI with the S-T slightly elevated and the T wave inverted. The normally conducted beats, although suggestive, are not diagnostic of an infarct. QS complexes with upright T waves in leads V₁, V₂, and V₃ may be seen in individuals without infarction. The abnormal left axis deviation, however, is suggestive of myocardial damage. Of particular interest in the broad Q wave followed by a negative T wave, occurring in the premature ventricular beat seen in lead V₃. This pattern, when seen in a ventricular premature beat, is further evidence of myocardial infarction.

Reprinted from New York State Journal of Medicine, Vol. 67, No. 17, September 1, 1967—Copyright 1967 by the Medical Society of the State of New York and reprinted by permission of Dr. Ira L. Rubin.

ON EPONYMY

Eponymy, the attachment to a phenomenon, structure, principle, etc. of the name of the describer or discoverer, is at least as prevalent in medicine as in any other discipline. The bewildering array of signs, syndromes, diseases, laws, operations, and anatomical structures so designated can be a source of fascination to the historically minded as well as of exasperation to the student and the practicing physician. Using Emmert's Law as an example in which the honor was misplaced, Campbell and Tauscher¹ have recently commented on some interesting aspects of eponymy and have reviewed some of the justifications advanced for its use.

Emmert's Law of 1881 relates the apparent size of an after image to the distance from the surface upon which it is projected. Campbell and Tauscher traced the origin of this law, and found a description of the principle involved in one of the translations of Schopenhauer's important philosophical work, "On the Fourfold Root of the Principle of Sufficient Reason". Schopenhauer in turn cited a paper by Seguin published in 1858, and the latter referred to another publication of the same year by Lubinoff, both of which contain statements of the principle in some form. Emmert's paper was published in a journal edited by Zehender, whose editorial comment in the same issue refers to his own earlier statement of the principle in 1856. Although the law is known by Emmert's name, it was described previously by at least four others. Multiple rather than single discovery seems to misplace the honor in this case. Such multiplicity of discovery occurs with great frequency in science, as noted by Merton.² Emmert made no other scientific contributions, and his eponym is a reward for neither priority or greatness, but an example of a class of proper nouns very prevalent in scientific communication.

Boring³ has maintained that the use of eponymy is a form of the "Great Man" interpretation of history. The use of great men's names can be considered as simplifying the details of discoveries and shortening their citation. The scientist's need for honor is gratified, and eponymy promises rewards and dominance for the ambitious. Merton⁴ points out, however, that the truly great men of science are those who make multiple contributions, and the attachment of their names to a number of them without further qualifying verbiage blurs specificity and causes confusion. Thus the greater the number of an individual's scientific contribu-

tion, the less useful is his eponym in scientific communication. It is the scientist of a somewhat lower echelon, who makes one major contribution, that provides the bulk of eponyms. Eponymy may thus be considered as a social-motivational system. The great man receives so much recognition for his multiple contributions that eponymy is superfluous, but the attachment of his name to his work spurs the lesser scientist on to continued effort, according to this view.

If one accepts the concept that science progresses by cumulative trial and error, then this progress will be dependent on the number of participants in scientific investigation. Although the greater minds are more likely to make multiple discoveries, the lesser scientists, being more numerous, can be expected to contribute a large number of additions to scientific knowledge. Specific eponymy may be one of the systems of rewards that social evolution has built into the structure of scientific society to stimulate its lower echelons.

This type of explication serves to clarify the eponymic process, but does not lessen the confusion and bewilderment that faces the physician when a syndrome is mentioned only by the describer's name and with no reference to its clinical nature. Despite the recognition that an eponym confers, most physicians would be happier with terms of reference that contained some descriptive clues as to the nature of phenomena.

Herbert Levine, M.D.

References

1. Campbell, D. T., and Tauscher, H., "Schopenhauer (?), Seguin, Lubinoff, and Zehender as Anticipators of Emmert's Law", *J. Hist. Behav. Sci.*, *II*: 58, 1966.
2. Merton, R. K., "Priorities in Scientific Discovery", *Am. Sociol. Rev.*, *22*: 635, 1957.
3. Boring, E. G., "Eponym as Placebo", in E. G. Boring, "History, Psychology, and Science", New York: Wiley, 1963.
4. Merton, R. K., "Singletons and Multiples in Scientific Discovery", *Proc. Amer. Phil. Soc.*, *105*: 470, 1961.

The Prognostic. It seems to me to be best for the physician to practice prognosis. For one who knows and declares in advance at the bedside, the present and the past and the things that are about to happen, the many things also that the sick man has left out, in telling his story would be counted on to know best the events of the illness; so that men would venture to trust themselves to this physician. And he would carry out his therapy best, knowing beforehand from the pathology of the present what is to come.—*Hippocrates*

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MD'S WIFE

What are you interested in? Art? Music? History? Sports? Books? Travel? Perhaps social action is your forte? Maybe you're just looking for new ideas for your group. Whatever you want, it's there in *MD's Wife*, and all as a part of a membership in the medical auxiliary. The medical family may be devoted to the advancement of medicine and public health, but its interests are as numerous as its size. Articles in the magazine are written by or about the doctors, their wives and families.

In September we joined a doctor's wife from Washington who visited her son in Vietnam, and another doctor and his wife who safaried to Africa, cameras in hand. If music is your interest, you might have liked to read about the Lyric Opera of Chicago and its general manager, a doctor's wife.

November brought thoughts of winter snows and Christmas gifts. Skiing in the Sierras with families of the Washoe County, Nevada auxiliary members, with colorful pictures to brighten the pages, was a "must" for sports enthusiasts. The treasure list of books for children from pre-school to 14 was a wonderful suggestion for Christmas giving and a big help to anyone who wanted to give an enduring gift. If you enjoy history, how about "The Women of Maywood" which also appeared in the November issue.

This is only the frosting on the cake for the really "sweet" articles are those of interest to all involved in medicine today. These are well-prepared comments on the health manpower shortage, youth learning about drugs and alcohol, sex education programs that have worked well, and successful urban action teams.

Connecticut has 3,762 members of the medical society and 997 members of the auxiliary. Doctor, what is your wife missing?

An Action Program to End TV and Movie Violence

I do not need to tell that the violence of our times is a threat to the well-being of every person in our nation—and especially our young people. Violence kills and maims as surely as does disease. It can irreparably blight our lives and darken the future of every young person unless we act to stop it.

As *McCall's* magazine recently pointed out, "Women can stop the outpouring of violence and sordidness on our television screens and in the motion-picture theaters." This is only one factor in the brutalization of our national life, but is it a factor we can do something about—*now*.

Much is being written about the situation—but not enough action is being directed at the sources of decision on programming and content. I propose that every auxiliary engage in an action program directed where it can do the most good. Here is what auxiliaries can do:

1. Appoint action committees in your auxiliary to call personally on:
 - Managers of all TV stations in your area.
 - Owners or managers of all local movie chains and individual theaters.
 - Heads of local advertisers on TV.
2. Form joint action groups with PTAs, Leagues of Women Voters, church women's groups, teachers.
3. Set up a viewing and screening schedule to monitor all shows, keeping records of the degree, frequency, time, etc., of violence on each station and in each theater. (Be careful *not* to give any appearance of censorship or of boycotting any given station or theater—this is not the tack we should take.)

(continued on page 207)



The Fortunate One.

Her urinary tract infection reveals itself through pain and discomfort.

While the pain and discomfort of a G.U. infection are anything but pleasant, the patient may be luckier than she realizes. That burning sensation (and/or frequency, urgency, dysuria) is a usually reliable sign of a urinary tract infection. And it's her good fortune that her infection won't go undetected...or untreated.

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Contraindicated in sulfonamide-sensitive patients, pregnant females at term, premature infants, newborn infants during the first three months of life, glomerular nephritis, severe hepatitis, uremia and pyelonephritis of pregnancy with gastrointestinal disturbances.

Warnings: Use only after critical appraisal in patients with liver damage, renal damage, urinary obstruction or blood dyscrasias. If toxic or hypersensitivity reactions or blood dyscrasias occur, discontinue therapy. In closely intermittent or prolonged therapy, blood counts and liver and kidney function tests should be performed.

Precautions: Observe usual sulfonamide therapy precautions including maintenance of an adequate fluid intake. Use with caution in patients with histories of allergies and/or asthma. Patients with impaired renal function should be followed closely since renal impairment may cause excessive drug accumulation. Occasional failures may occur due to resistant microorganisms. Not effective in virus and rickettsial infections.

Adverse Reactions: Headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, Stevens-Johnson syndrome, injection of the conjunctiva and sclera, petechiae, purpura, hematuria or crystalluria may occur, in which case the dosage should be decreased or the drug withdrawn.

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How Supplied: Tablets, bottles of 50.



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Woman's Auxiliary (Continued from 205)

4. Feed this information steadily to the local TV critics, editorial writers and movie reviewers as background for their commentaries.
5. Launch letter-writing campaigns to the presidents of national advertisers, TV networks, advertising agencies and movie producers. Emphasize the auxiliary's concern for sound health education; avoid abusive language or threats of boycotts. Here are some addresses you can write to:

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30 Rockefeller Plaza, New York City

Leonard Goldenson, President
American Broadcasting Company
1330 Avenue of the Americas
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Frank Stanton, President
Columbia Broadcasting System
51 West 52nd Street, New York City

Jack Valenti
Motion Picture Association of America
522 Fifth Avenue, New York City

6. Support community forums on violence and urge other women's groups to participate.

I urge you to give top priority to this campaign among your current activities. Keep national auxiliary headquarters informed of the response to your action program (including copies of letters sent and received) so that we may gauge the overall effectiveness of our efforts.

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OBITUARIES

Rudolph Maslak, M.D. 1901-1968

Dr. Rudolph Maslak, 67, of South Main Street, Warehouse Point, East Windsor, Connecticut, died suddenly Wednesday, October 30, 1968.

A lifelong resident of East Windsor, he attended Mount Hermon School for Boys, Mount Hermon, Massachusetts, received his pre-medical training at the University of Illinois, and graduated from the University of Louisville School of Medicine.

He interned at the Lawrence and Memorial Hospitals in New London, under the late Dr. John Satti, who remained one of his closest friends until the latter's death a few years ago.

Dr. Maslak opened his office for the practice of medicine in Warehouse Point in 1935 and practiced there for 33 years. He formerly served as an Assistant Health Officer of the Town of East Windsor and during World War II served as the town's Medical Examiner.

Dr. Maslak was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the Connecticut Academy of General Practice, and the American Medical Association. He was a communicant of the United Methodist Church of Warehouse Point, and a member of the East Windsor Grange.

Surviving are his wife, Gladys Maslak; a son, Gary; two brothers, Emil and Joseph, both of Windsorville; and a sister, Mrs. Mary M. Reynolds of Eagleville, Connecticut.

Edward A. Palomba, M.D.

Earle G. Haliday, M.D. 1903-1968

Dr. Earle G. Haliday, 65, of 168 Water Street, Stonington, Connecticut practiced medicine here since April, 1933. He died unexpectedly December 31, 1968 in Falls Church, Virginia where he was visiting his son, Lieutenant Commander George Haliday, USN.

Dr. Haliday was born in Cavanville, Ontario, Canada, September 1, 1903, son of George and Blanche (Smith) Haliday. He graduated from Queen's University, Kingston, Ontario, in 1927.

Dr. Haliday moved here from New York where he had practiced medicine after completion of his internship in Cleveland, Ohio.

The only interruption in his local practice came during World War II when he spent three years as a flight surgeon, serving in the Pacific Theater with the United States Army. He completed his military service in 1945 as a major.

As Vice Commander of the Stonington Ambulance Corps, Dr. Haliday had long been interested in the ambulance service, and devoted many hours to the instruction of members.

He was a member of the staff at the Westerly Hospital in Westerly, Rhode Island, a member of the Connecticut State Medical Society and the American Medical Association. He was also a member of the Thames Club of New London and the Wadawanuck Club.

Besides his wife Martha, and son, Dr. Haliday leaves a daughter, Mrs. Frank Zechlin of Arlington, Virginia; two sisters, Mrs. Kathleen Greenwood of Toronto and Mrs. Edgar Dollman of Peterborough, Ontario, and five grandchildren.

In a more personal vein, I would like to add my tribute. I have known "Dooley," (his only nickname) ever since he came to Stonington thirty-six years ago. Besides being a good physician and real friend, we have spent many happy hours bowling and golfing. He will be sorely missed in the town of Stonington.

William T. Veal, M.D.

In Memoriam

Foster, Lewis C.—New Haven, Harvard Medical School, 1923. Dr. Foster was professor emeritus of surgery at the Yale Medical School and Attendant Surgeon at the Yale-New Haven Hospital. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, the American Medical Association, the American Board of Surgery, the Universal Surgical Society, and the American College of Surgeons. Dr. Foster died February 9, at the age of 72.

Mastroianni, Luigi—New Haven, Padway University School of Medicine (Italy), 1917. Dr. Mastroianni was a general practitioner in New Haven for over 30 years. He was a member of the New Haven County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. Mastroianni died February 3, at the age of 77.

Artists — Attention!

GENERAL INFORMATION: The Connecticut Physicians Art Association is planning the 1969 Art Exhibit in conjunction with the annual meeting of the Connecticut State Medical Society. The following information is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Conn.

WHEN: May 13, 14, 15, 1969

ELIGIBILITY: Physicians (members of Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor.) All previous exhibitors are invited to show their works at this meeting, and new exhibitors are welcomed. Works eligible will include oil, water color, tempora, black and white etchings, photography, pastels, collages, mixed media and sculpture. Paintings over 24 x 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories; 1. children under 16 yrs. (children over 16 yrs. will be judged with adults); 2. beginners; 3. intermediaries; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

Under no condition can art work be accepted after MAY 11th.

COST: A hanging fee of two dollars (\$2.00) will be charged for each entry and fifty cents (\$.50) for children under 16 yrs. with two entries per artist. (Space requirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the entry blank should be submitted to me at the below listed address with your check prior to April 30, 1969. The other half should be attached to the picture. Make checks payable to Connecticut Physicians Art Association. Please fill in entry blanks com-

pletely so that entry can be categorized easily in the above noted four divisions.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, May 11, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, May 15, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society, the hotel, (nor the Art Association) can assume no responsibility for loss or damage of any cause to art works.

If further information is needed, the following persons may be contacted:

Stewart J. Petrie, M.D., President, 56 Minerva St., Derby, Conn.; Mrs. Orvan Hess, Vice President, 29 Old Orchard Rd., North Haven, Conn.; Mrs. John Shoukimas, Chairman, Art Committee, Woman's Auxiliary, CSMS, 26 Pheasant Hill Dr., West Hartford, Conn.; Edward Williams, M.D., 580 Hillside Ave., Naugatuck, Conn.; Herman Austrian, M.D., 935 White Plains Rd., Trumbull, Conn.; Donald Morrisson, M.D., 26 Birch Rd., West Hartford, Conn.; Eugene Rightmyer, M.D., 114 Sherman Ave., New Haven, Conn.; Mrs. Mark Hayes, 163 Ridgewood Ave., North Haven, Conn.; Mrs. John D. Murphy, 8 E. Normandy Dr., West Hartford, Conn.; Mrs. Henry Sherwood, Penfield Hill Rd., Portland, Conn.; Mrs. Clifford Wilson, 19 East Town St., Norwich, Conn.

From the reports, comments and compliments received from the past years' shows, this seems to be a point of major interest of the annual meeting of the Connecticut State Medical Society. We therefore wish to thank the art hobbyists and encourage their continued participation in this exhibit.

Stewart J. Petrie, M.D., *President*
Connecticut Physicians Art Association

BOOK REVIEWS

GROWTH OF THE NERVOUS SYSTEM. *Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1968. 295 pp. with 101 illustrations. \$12.00.*

Reviewed by: LOUIS H. NAHUM

The brain is infinitely complex more than is the whole universe. With its 30,000 million cells and their bewildering connection, it is obvious that research upon it can no longer be carried out by neurophysiologists and neuroanatomists alone but by many disciplines working on many levels. In this volume there is a merging of the data from the different disciplines all studying the development of the nervous system and its relation to the maturing of specific end organs in the adult animal.

The contributors explore subjects such as neural connections, the development of movement, the role of chemical signals and tropic interactions. Relation of the emerging knowledge to clinical problems such as for example neuromuscular malfunction will interest people in these fields.

As this book demonstrates, techniques for exploring the nervous system have been considerably refined. The use of radioactive tracers and electron microscopy, newer methods in neurochemistry tissue culture transplantation and immunology allows for deeper probes into the mysteries of the nervous system that were not possible in the past. The new data that have emerged from this symposium make this book essential reading for keeping up to date and pointing to the areas in which new research is needed. It should be read by neurologists and neurosurgeons, by psychiatrists as well, not to speak of neuroanatomists and neurophysiologists.

ANTILYMPHOCYTIC SERUM. *Ciba Foundation Study Group No. 29. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, 1967. 165 pp. with 37 illustrations.*

Reviewed by: STUART C. FINCH

This short monograph includes all of the papers and discussions from a recent CIBA Foundation Symposium devoted to the use of antilymphocyte serum as an immunosuppressive agent. The participants of this Symposium included not only some of the world's most outstanding immunologists but also some leading surgeons in the field of organ transplantation. Each of the seven papers presented is followed by an uninhibited discussion of the issues raised. Although much of the discussion is speculative many pertinent references are cited. The program participants generally agreed that heterologous antilymphocyte serum now represents an important and potent form of immunosuppressive therapy. Limited experience in man suggests that it is effective and safe when used either alone or as adjuvant therapy. Most of the Symposium members encouraged further evaluation of antilymphocyte serum in man in the fields of autoantibody diseases and organ transplantation. This monograph on anti-

lymphocyte serum is of considerable value to investigators in these fields, but to most others it probably is too specialized to be of great interest.

HEALTH OF MANKIND. *Ciba Foundation 100th Symposium. Edited by Gordon Wolstenholme and Maeve O'Connor. Little, Brown and Company, February 1968. 297 pp. \$12.00*

Reviewed by: EDWARD M. COHART

The Ciba Foundation holds five or six conferences a year, each lasting three or four days and usually focusing on research topics of current interest. For this, its 100th symposium, the Foundation undertook a much broader assignment, a consideration of world health.

Twenty eight students of various aspects of world health met to discuss fourteen papers presented by their members. This book is a record of the presentations and discussions. The distinguished participants included representatives of the biological sciences, medicine, epidemiology and public health, and architecture and urban planning.

The subject is divided into three major rubrics: assessment of the present health of mankind, major factors aggravating world health problems, and manpower and education. Stress is placed upon the essential fact that health is a characteristic of man in society that is both the result and the cause of other characteristics and that therefore it is of great concern to more than the health professional. This is something we often find difficult to appreciate in our highly developed nations, but it is all too obvious to us in many developing countries.

Discussion of the present health of mankind is concerned with the incidence and prevalence of physical and mental health, the validity of world data, and measures that can be taken to improve both the quality of the data and our understanding of the conditions described by these data. Considered among the major factors aggravating world health problems are matters of population growth and age distribution, food supply and nutrition, pollution of water, air, and food, political and cultural barriers to health, and the many problems created by urbanization. The size, distribution, education and training of health professionals and other health personnel and an outline of a possible world health service as an administrative vehicle for making better use of the available health manpower bring the symposium to a close.

This book might well serve as an introduction to many aspects of world health for the health professional or the educated layman, even though its coverage is by no means complete and its emphasis somewhat uneven. It can also be read by the student of world health in a more selective fashion if he approaches the volume with the expectation that he will find therein a series of essays on different aspects of world health approached from a number of points of view.



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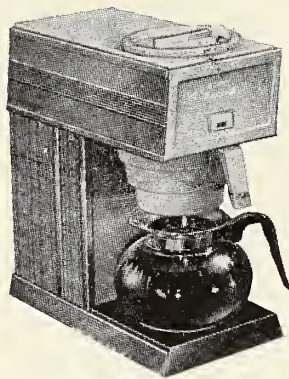
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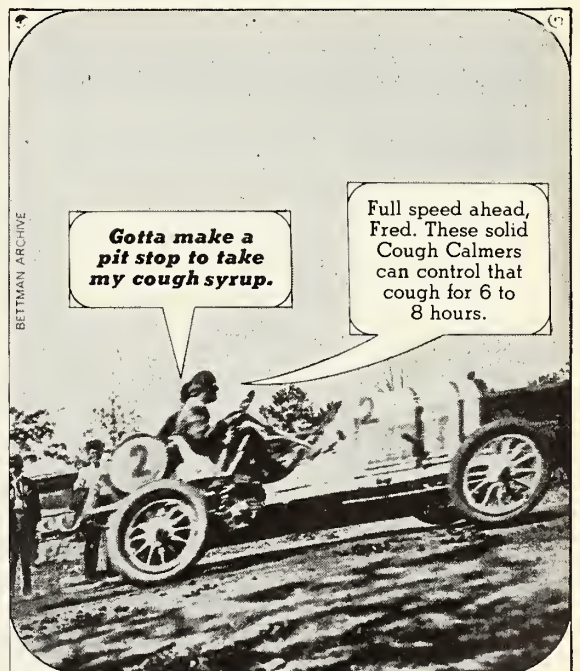
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SYNOPSIS OF SURGERY. Edited by Richard D. Liechty, M.D. and Robert T. Soper, M.D. The C. V. Mosby Company, St. Louis, 1968. 1091 pp. With 346 illustrations. \$12.50.

Reviewed by: IRA S. GOLDENBERG

Medical texts serve varied functions and are written for diverse audiences: some attempt to cover a broad area of medicine, such as general surgery or pediatrics, through a group of contributors; others seek to define a small area with precision by concentrating on the details of a specialty interest. The former are, of necessity, somewhat superficial because of the vast amount of material involved and the latter are of obviously restricted usefulness. And which type best suits the needs of a medical student, house officer or non-specialist in the field being covered? This hypothetical question with no possible unqualified answer has given rise in recent years to a group of "synopsis" books designed to meet the median need of these groups.

In *Synopsis of Surgery*, Drs. Liechty and Soper cover only the core of our knowledge of surgery, i.e., the essentials, and they make no other claim. The book thus appeals mainly to the student or non-surgeon who is seeking a broad concept of diagnosis and therapy of surgical diseases. The authors succeed admirably, for in this small volume (by page size rather than pagination) they have covered all aspects of modern surgical practice without detail or controversial dissertation. The contributors are well chosen. There are many illustrations and each adds significantly to the topic under discussion. This book is recommended to a limited segment of physicians and physicians-to-be: those who seek subtleties, however, must find another source.

ATLAS OF STRABISMUS. Edited by Gunter K. von Noorden, M.D. and A. Edward Mauwenee, M.D. The C. V. Mosby Company, St. Louis, 1967. 115 illustrations, 29 in color by Robert B. Wingate, M.S., F.R.S.A., 188 pp. \$17.50.

Reviewed by: MARVIN L. SEARS

This book is unique as a well organized, well balanced compilation of basic information regarding sensory and motor anomalies in strabismus. The approach to the patient with strabismus and the interpretation of results of examinations are clearly presented with illustrations and minimum necessary verbal text. The subject is subdivided into seven categories: each is covered by one section of the book.

The first section describes the anatomy of the extraocular muscles and their physiologic action. The second section covers "pseudostabismus," and contains a discussion of the differential diagnosis of the decentered corneal light reflex.

The third and fourth sections deal with qualitative and quantitative diagnosis of strabismus. Techniques described are more comprehensible to the person who has first hand experience evaluating patients for strabismus than to the uninitiated.

The fifth section, on sensory anomalies, reflects the authors' interest in this area. Illustrations for amblyopia and for tests for anomalous retinal correspondence are excellent. The sixth section concerns the diagnostic evaluation of a number of anomalies of motor status. The authors feel that A and V patterns are predominantly found in association with overaction of the oblique muscles, however, they recognize some cases where oblique muscle anomalies are not present. (Figure 101-A, in the section on A & V patterns, shows the inferior oblique muscles arising from the temporal side of the orbit. Page 82—Amblyopia spelled wrong. Contradiction)

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LIFE OR DEATH: ETHICS AND OPTIONS. *Essays by Edward Shils, Norman St. John-Stevas, Paul Ramsey, P. B. Medawar, Henry K. Beecher, Abraham Kaplan. Introduction by Daniel H. Labby. Reed College, Oregon. University of Washington Press, Seattle and London, 1968. 167 pp. \$4.95.*

Reviewed by: LOUIS H. NAHUM

This symposium on the Sanctity of Life was presented at a time when an unpopular, unwanted and futile war was threatening to escalate insanely, and the use of nuclear power in war was a worldwide anxiety. The problems of racism and rioting were again aflame, the wounds of the thalidomide tragedy were still unhealed and contraception and abortion were troublesome moral dilemmas. It was time to explore the ethics and options controlling the powers over life and death. Is life more or less valuable today than ever before? How do we identify the forces in society that determine how valuable one man holds the life of another? What guide-lines exist in law; theology or in the liberal arts? Are biomedical sciences dedicated to preserving health and prolonging life taking undue liberties in the guise of improving man's condition.

In the scientific area some of the numerous threats to life are easily identified: contraception, abortion, eugenics, euthanasia, drug testing, experimentation on man. The parallel questions of morality in the employment of these powers were first explored. Has the growth of moral thoughts been consistent with the explosion of scientific knowledge? The moral dimension of medical practices have always been carefully nurtured; the value of human life, the basis of human dignity, the goal of human existence and the corollary duties of medicine have always been governed by moral dimensions.

Law being the prime and stable principle of continuity of our society is the first specific and enforceable limitation science and medicine encounter. The power of science and the limitations of the law and social order suggest that the privacy and the rights of the individual should be considered by a sociologist. Likewise religion and philosophy must enter and contribute to a consideration of the sanctity of life. What is the role of religious principles in guiding human behavior. The philosopher, of course, is to furnish the final common path—reason, arbitration, common sense if not pure logic. Thus was this symposium conceived.

There are so many questions that remain, like the morality of killing in war, the question of conscientious objection, capital punishment and the right to take a life, planned genetics and the control of the quality of life and many others. Thus it was recognized that there would be many other conferences of which this one would be the first of a series.

The power of science has been gathering momentum since the Industrial Revolution and now is of a magnitude never before witnessed. Serious questions arise as moral imperatives: for what purpose and to what ends shall power be emphasized? Biologists are aware of the rapidly growing ability of their fellow human beings to alter the face of the earth through technology. Such alterations can bring about far spreading and often destructive changes in the web of life. Our technology has outpaced our wisdom, our cleverness has grown faster than our wisdom. Where does anyone derive the right to pollute the air we all breathe, the water we all need, the land upon which all our life depends.

Professor Shils' credo is that if life were not viewed and experienced as sacred then nothing else would be sacred. Norman St. John-Stevas the barrister and member of Parliament proclaims that Law both reflects and preserves the normal consensus of society. He identifies that the concept of the sanctity of life is basic to law. He then occupies himself principally with the problem of abortion and to a lesser extent euthanasia, suicide and capital punishment. Man is not absolute master of his own fate but holds his life and body in trust for other purposes. These concepts preserve his humanity by erecting barriers beyond which technology cannot pass.

Professor Ramsey tries to make out a strong case against abortion on religious grounds without considering any of the scientific advances of genetics which makes the quality of the offspring predictable. Medawar emphasizes the importance of disposing of quantitatively poor and monstrous genetic material (we can now easily determine in utero the growth of a mongoloid fetus for example).

Dr. Beecher discusses the ethical problems arising in experimentation on man. To the consideration of the moral dilemma: experiment only on one patient. If for his benefit then all is right. It is wrong when the experimental subject is manipulated not at all for his specific benefit but hopefully for the benefit of patients in general. This opens the possibility of breaches of ethical conduct in experimentation. To protect the patient and safeguard the morality, Dr. Beecher would insist that there be "informed consent" and "an intelligent, skillful, compassionate and responsible investigator" and much more.

The final remarks by Professor Kaplan were brilliant, thoughtful, penetrating and graceful a remarkable extemporaneous document. Kaplan says of himself "I am by training a positivist, by inclination, a pragmatist, in temperament a mystic, in practice a Democrat; my faith Jewish, educated by the Catholics, an habitual protestant, born in Europe, raised in the midwest, hardened in the East and softened once more in California." It is not surprising that Professor Kaplan recognized as one of the most thoughtful and articulate of contemporary philosophers, summarizes the preceding discussions and comments on what was not said as well as on what was said.

One senses that the contributors have well established their unique competence to deal with the difficult questions at hand. It is an edifying experience to read and reread the individual chapters.

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Response to Exercise After Bed Rest and After Training. American Heart Association Monograph Number 23. Edited by Bengt Saltin, M.D. et al. American Heart Association, Inc., 44 East 23rd Street, New York, New York, 10010, 1968. 78pp. \$4.00.

MEETINGS

GENERAL

March 27

185th Annual Meeting, New Haven County Medical Association

Waverly Inn, Cheshire

Business Meeting 3:00 P.M., Dinner 7:00 P.M.

April 9

177th Annual Meeting, Hartford County Medical Association

Hartford Hilton Hotel

Business Meeting 5:00 P.M., Reception 6:45 P.M., Dinner 7:00 P.M. Speaker, Norman Cousins, Editor, Saturday Review

April 15

177th Annual Meeting, Fairfield County Medical Association

Frederick's, Fairfield

Business Meeting 4:00 P.M., Dinner 7:00 P.M.

May 13, 14, 15

177th Annual Meeting, Connecticut State Medical Society

Hartford Hilton Hotel

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospitals, New London

April 8 7:15 P.M.

Biochemistry, Physiology and Disorders of Muscle

David M. Dawson, M.D., Associate in Neurology
Harvard Medical School

April 22

Normal and Abnormal Vision

H. Richard Tyler, M.D., Assistant Professor of Neurology, Harvard Medical School

CANCER

Oncology

Sponsored by the Connecticut Division of the American Cancer Society and the Yale Medical School.

Speakers: Yale Medical School

Russ Home Conference Room, Griffin Hospital, Derby

April 1 8:00 A.M.-9:00 A.M.

Management of Patients with Lymphoma

Ronald DeConti, M.D., Assistant Professor of Medicine and Pharmacology

Chairmen: Dr. DeConti; Vincent A. DeLuca Jr., M.D., Assistant Clinical Professor of Medicine

Open to all Physicians

May 8-10

National Conference on Breast Cancer

Shoreham Hotel, Washington D.C.

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MEDICINE

Wednesdays 12:00 P.M.-1:15 P.M.

Pulmonary Diseases and Pulmonary Physiology

Radiation Center Conference, Room, Hospital of St. Raphael, New Haven

Chairman: John B. Berte, M.D., Director, Department of Pulmonary Diseases and Inhalation Therapy, Hospital of St. Raphael

Open to all physicians

Thursdays 1:30 P.M.-3:30 P.M.

Hematology

Hematology Laboratory and Wards, Hospital of St. Raphael, New Haven

Robert P. Zanes, Jr., M.D., Hospital of St. Raphael

Open to all physicians

March 26 **9:00 A.M.-3:30 P.M.**

Annual Symposium, Kidney Foundation of Connecticut

Veterans Hospital, West Haven

Lupus Nephritis in Children and Adults: Natural Cause and Therapy, Naomi Rothfield, M.D., Associate Professor Of Medicine, University of Connecticut School of Medicine

Recent Advances in Renal Physiology, Gerhard Giebisch, M.D., Professor and Chairman, Department of Physiology, Yale Medical School

Potassium Balance and Renal Acid Secretion in Health and Disease, W. Gordon Walker, M.D., Associate Professor of Medicine and Chief, Renal Section, Johns Hopkins University Medical School

Registration fee, \$10 including Lunch; open to all physicians

March 12-28

Clinical Management and Control of Tuberculosis

Batley State Hospital, Rome, Georgia

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March 28-29

The 3rd National Congress on the Socio-Economics of Health Care

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May 24

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PEDIATRICS

May 21

Scientific session sponsored by the New England Pediatric Society and New Haven Area Rehabilitation Center

Speakers: Yale Medical School, Viral Infections in Pregnancy as a Cause of Fetal Damage, Dorothy Horstman, M.D., Professor of Epidemiology and Pediatrics; The Effects of Maternal Analgesic Agents on the Fetal Heart Rate, Edward Hon, M.D., Associate Professor Obstetrics and Gynecology; Recognition of Minimal Brain Damage in Early Infancy, Sally Provence, M.D., Professor of Pediatrics; Minimal Brain Damage-Conceptions and Misconceptions, Ethylyn Klatskin, M.D., Assistant Professor Of Psychology; Behavior of the 'Brain Damaged' Child; John Schowalter, M.D., Assistant Professor of Pediatrics and Psychiatry. Early Educational needs of the Deaf Child, David Green.

SURGERY

Anesthesiology

March 15

10th Annual Postgraduate Anesthesia Seminar of the New Jersey State Society of Anesthesiologists

Cherry Hill Inn, Cherry Hill, New Jersey

Registration fee, \$14 including lunch. Hospital interns and residents in anesthesiology admitted without charge

Connecticut Medicine

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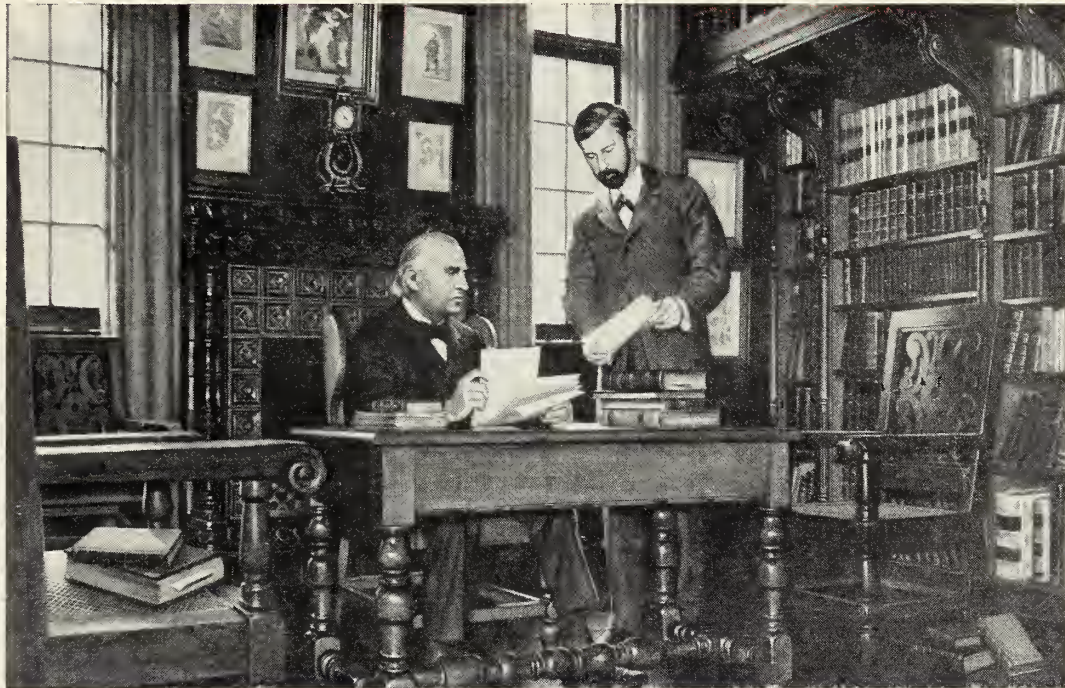
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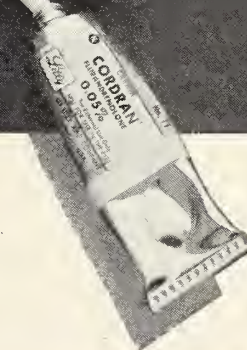
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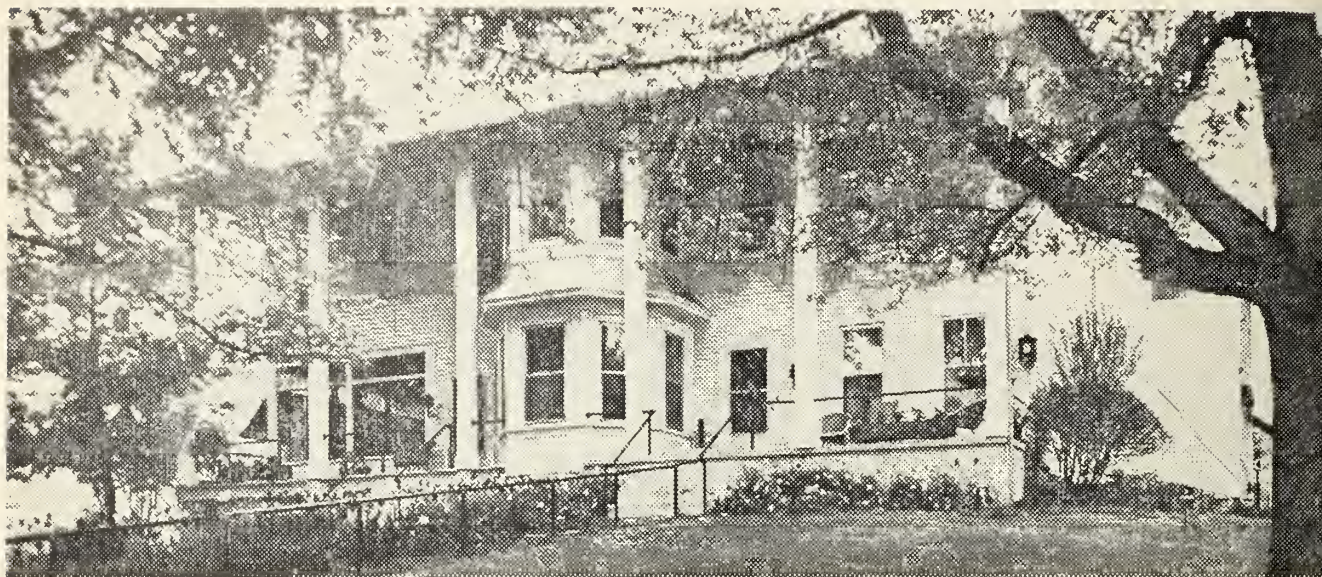
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Science Tools: 29. The Proton Beam Radiation Treatment In Acromegaley

Lawrence et al¹ were the first to point out the peculiar merit of the proton beam for radiation treatment of human disease when the target area is deep, circumscribed and identifiable and showed its applicability to the pituitary region especially. Up to 1966, forty-seven acromegalic patients were treated by a rational or cross fire technique delivering up to 4000-9000 rads to the sella area.² Kjellberg, a neurosurgeon, experienced in stereotactic techniques in collaboration with two physicists, W. Preston and A. Koehler, who knew how to generate and control the proton beam within a precise part of the intracranial volume desired, have now successfully treated a goodly number of patients.

The instrument devised for producing the proton beam used in acromegalics is 160 million electron volt (Mev.) Harvard cyclotron. After a careful preoperative evaluation including a pneumoencephalogram, visual fields and extraocular motor function, the premedicated patient is taken to the cyclotron and a stereotactic head frame is affixed to the skull under local anesthesia. The proton beam is aligned with the pituitary fossa and confirmed by exposure to a polaroid film to an X-ray source and to the proton beam.

There is a specially valuable feature of the heavy proton particle namely that those of a given energy all stop at about the same point in tissue giving up a markedly greater amount of destructive energy in the last centimeter or so before they reach the

stopping point to display the so-called "Bragg peak" of linear energy transfer. Even if only one portal is used the Bragg peak permits the concentration of a dose in the deep target with no radiation beyond it. If one centers the beam in the anterior portion of the sella turcica, the visual pathways are spared and so is the posterior lobe. There are, however, small corrections that have to be made to account for the passage of the beam through brain, other soft tissues and bone on the side of the head.

The acromegalics receive rays from six portals of entry on each side of the head. These portal diameters range between 7-15 mm. to accomodate varying sizes and shapes of the anterior pituitary adenoma. The entire proton beam treatment is completed in approximately one and one-half hours during which the patient is awake and responsive. They then remain in the hospital two to three days. There is only trivial scalp tenderness at the site of the drill rad applications. Then there are follow-up evaluations which include complete pituitary function, neurologic survey at six months and a year thereafter.

Before the method was perfected the first case upon whom the proton beam was used developed serious unilateral visual loss. Only one case developed anterior pituitary insufficiency. There were no deaths, no cerebrospinal fluid leaks or infection or posterior pituitary insufficiency such as diabetes insipidus. Thus Kjellberg demonstrated on his series of cases that they can give hypophysial doses of 10-12000 rads with a remarkable degree of safety. With the revised technique they treated forty-three

THE COVER

CHARCOT: MASTER OF NEUROLOGY

GREATEST neuroloist of the 19th century, Parisian physician Jean-Martin Charcot (1825-1893) developed La Salpêtrière from an asylum for indigent women to one of France's leading hospitals. Charcot's study and care of its vast patient population led to teaching, research, and the creation of the world's leading neurological clinic; attracted students from many nations; raised neurology to a respected medical science. Some of Charcot's teachings inspired Sigmund Freud of Vienna (Charcot's student, 1885-1886) to develop the world-famous Freudian hypothesis on psychoanalysis and psychotherapy.

successive patients with no significant complications whatsoever during the three year period in which they have been in action. Their total experience with pituitary radiations with proton at the Bragg peak now comprises over 200 patients. With the radiation given in a single dose and the fact that only 2-3 days in the hospital are required thereafter, emphasizes the minimal stress to the patient and the low financial outlay involved.

The principal disadvantage of the method of proton beam destruction of the pituitary gland is the many months required for the full extent of the injury to materialize. But in the great majority of patients with acromegaly this is almost immaterial. Of course, the ideal is to be able to stop the hormonal disorder of the acromegalic patient's eosinophile adenoma without disturbing the normal function of the other hormone producing cells of the anterior pituitary lobes. They may, however, be obliged in some patients to produce deficits in the other cells to obtain a more consistent profound drop in production of the growth hormone. Four of their patients showed no decline in growth hormone production and in two there was even a slight increase. Doubtless either larger doses to begin with or repeat therapy may lead to other deficits but these are now easily replaceable.

Kjellberg's studies to date, however, suggest that heavy particle radiation of the pituitary will become increasingly useful and popular.

L.H.N.

References

1. Lawrence, J. H., Tobias, C. A., Born, J. L., Linfoot, J. A. and D'Angio, G. J.: Heavy particles in experimental medicine and therapy. *JAMA*, 196: 166, 1966.
2. Kjellberg, R. N., Shintani, A., Frantz, A. G. and Kliman, B.: Proton-beam therapy in acromegaly. *New Eng. J. Med.*, 278: 689, March 28, 1968.

The Conquest Of Malaria

At the onset of World War II quinine and quinacrine (atabrine) were the drugs of choice to treat malaria. Because quinacrine stains the skin yellow and at times causes gastrointestinal distress, something better was needed. Out of much experimentation and screening there came chloroquine and pyrimethamine (daraprim). Chloroquine remained the most effective until an outbreak of chloroquine resistant falciparum malaria. Now we have come to realize that there exist sharp differences between strains of the same species of parasite as well as their similarities. Screening of drugs against many animal species led to many

new and effective drugs, although it became apparent that each of them including chloroquine had specific limitations and no one drug solved the whole problem.

Chloroquine for example cannot destroy tissue schizonts and therefore after "cure" by chloroquine, relapses can and often do occur. It does destroy the gametocytes except in falciparum. Malaria, hence its use alone produces carriers of malignant malaria. Pyrimethamine was sometimes curative of falciparum, occasionally in vivax but not only was it too toxic, but it rapidly led to development of resistance. There are apparently many strains of *P. falciparum* with considerable variation in virulence. It also differs from the other types of malaria in the nature of its response to drugs.

If falciparum infection responds well clinically most patients are cured and are not likely to suffer relapse. In all other forms even the best clinical response is likely to be followed sooner or later by relapse. The reason is that falciparum does not form secondary tissue schizonts while the other forms do. In malaria with secondary tissue schizonts when suppressive therapy is discontinued an erythrocyte phase of the cycle sooner or later develops and acute malarial relapses occur. Thus a dose of chloroquine which ameliorates the acute attack of falciparum cures the patient for good.

Once this problem was recognized, a program for the development of its effective treatment was undertaken at Walter Reed Army Institute of Research. Here they already had at their disposal greater knowledge of the metabolic processes of the parasite, newer approaches to toxicity of drugs in man and the much larger number of strains of avian and mammalian plasmodia and *P. falciparum* experimentally transmitted to the chimpanzee and gibbon. In nearly four years 110,000 chemicals were screened mostly with negative results, but they found one treatment they were looking for. It came from the studies on how pyrimethamine acts, it has depressant action on folic acid.

All folic acid depressants however have their limitations, because they are a serious threat to formation of blood in man. Depression of folic acid would be defensible as a therapeutic approach in malaria only if some means of protecting the human host were developed. Pyrimethamine's effect on malaria is by its folic acid depression. Here further studies with sulfonamides come in. They also have a mild anti-malarial action through their "antifol" effect. Fortunately the sites of action of

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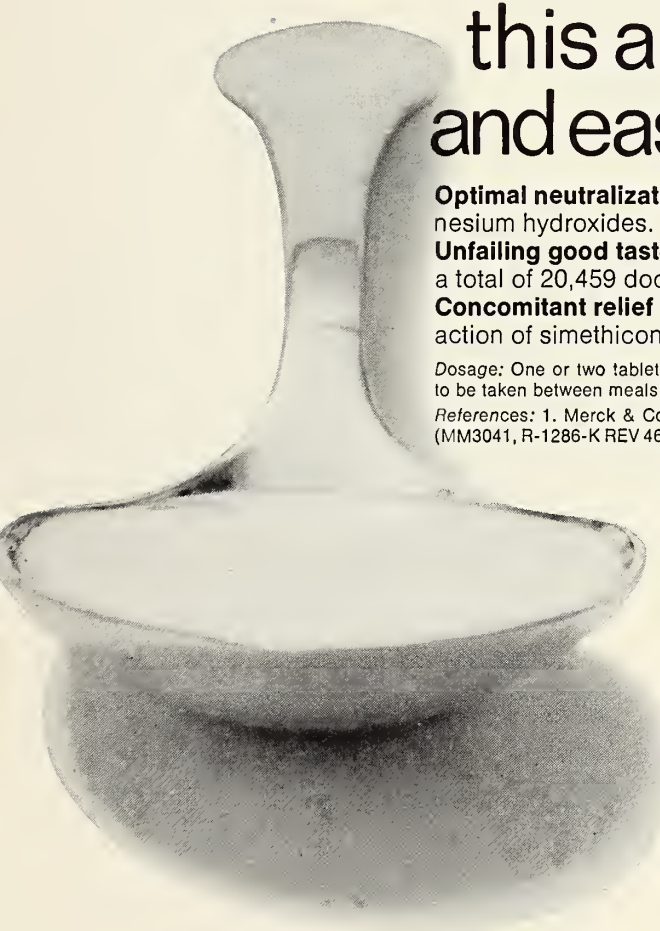
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References: 1. Merck & Co., Merck Chemical Division: Antacid Literature Survey, Rahway, New Jersey. (MM3041, R-1286-K REV 463.) 2. Danhof, I.E., report on file. 3. Hoon, J.R.: Arch. Surg. 93:467 (Sept.) 1966.



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these drugs differed and the combination it was thought should make them more effective against the parasite but also safer for man.

Sulfonamide prevents synthesis of folic acid from para-aminobenzoic acid. Pyrimethamine on the other hand prevents conversion of folic to folinic acid by depression of the enzyme dehydro-folic acid reductase. Such an action develops in man as well as in the parasite. Fortunately the two sites of the two step depression are present only in the parasite. Therefore the combination was a far greater threat to the plasmodium than to man in whom only the second step occurred. This combination turned out to be equally effective in the therapy of coccidiosis, toxoplasmosis and is even effective also against some bacterial infections as well.

The next step was to search for better drugs in each category. A substitute for sulfonamide was desirable because it is highly protein-bound and feeble in action. The eventual choice was sulphalen having extremely long duration of action, a half-life of 65 hours and much less protein-bound. This sulpha derivative could be counted on for long continued intense action on the parasite and in addition causes no complications. A substitute for pyrimethamine was also needed because tolerance to it had developed in the field. It was found in trimethoprim which seems not to induce tolerance, is less toxic than pyrimethamine and is a very effective "antifol" in protozoa. Thus it provided an ideal second stage for the "antifol" action weak in man and potent in protozoa.

The combination was soon tried on human volunteers with dramatic results and then tried in Vietnam with outstanding success. One dose cures in almost all cases and the one dose combination of the two drugs contains much smaller amounts of either drug than has a clinical or toxic effect alone. This phase of the battle against falciparum malaria seems to be a clear cut victory. However, a prophylactic drug is still needed because regular use of folic acid depressants as a prophylactic could eventually depress blood formation in the human host. There is also the possibility of rapid development of resistance as well as tolerance. Perhaps there will be an immunologic solution since we know resistance to malaria does develop in animals and man.

One finding is disturbing because as troops return from Vietnam with a new parasite which travels rapidly we also have a new potential reservoir for infecting mosquitoes. All the troops are

given primaquine to destroy gametocytes which they may harbor whether or not they had clinical disease to prevent them from returning as carriers of chloroquine resistant *P. falciparum*. Obviously the treatment of chloroquine resistant malignant malaria does not end at the battlefield as our soldiers bring back a Vietnam legacy to the home front.

The current military attack on malaria has solved a problem in medicine that will benefit all mankind. To date this is our only real victory in Vietnam.

L.H.N.

References

1. Model, W.: Malaria and victory in Vietnam. *Science*, 162: 1346, December 20, 1968.
2. Martin, D. C. and Arnold, J. D.: *JAMA*, 203: 476, 1968.

The Ballistocardiogram, A Superior Predictor Of Coronary Artery Events

There is ample evidence that the ballistocardiogram (BCG) is a measure of myocardial strength. Numerous studies on animals, simulations of systole in cadavers, experiments made on electronic circulatory models and finally studies on man constitutes the evidence. The easily obtained BCG force record reflects the acceleration with which the myocardium ejects its stroke volume and, therefore, provides unique information about myocardial contractility. Early in Starr's BCG career¹ he noted two important findings. One was that the records of normal youth are monotonously similar and highly reproducible, in both amplitude and wave form. This was the basis for his belief that the deviations observed in the clinic are the result of physiological variability.

The BCG's become smaller and of bizarre form as age advances so the circulatory system of the aged does not usually perform like that of youth and the BCG record provides a measure of this change. Many years ago Starr began a prospective study of people and found that BCG abnormalities in previously healthy persons often foretells not only the development of one of a number of unrelated circulatory abnormalities, but it also carries with it a considerably greater death rate in those already afflicted with circulatory disease. Now it can be stated unequivocally that abnormality of the BCG wave form strongly correlates with the onset of coronary heart disease (CHD).²

Starr's preliminary observations led Baker and his associates³ to focus their BCG studies specifically upon CHD. As a result two important impres-



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Indications: Infections susceptible to oral penicillin G; prophylaxis and treatment of streptococcal infections, treatment of pneumococcal, gonococcal, and susceptible staphylococcal infections, prophylaxis of rheumatic fever in patients with a previous history of the disease.

Contraindications: Infections caused by nonsusceptible organisms; history of penicillin sensitivity.

Warnings: Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia.

In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.

Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.

Adverse Reactions: (Penicillin has significant index of sensitization): Skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis, urticaria, serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").

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sions were soon established as fact: that patients with CHD more frequently have BCG abnormalities than do comparable controls, and that abnormalities are excessively rare in young controls. It was further observed that with advancing years both patients and controls acquire increasing BCG abnormalities so that it is as common in aged controls as it is rare in the young. These findings could mean that when BCG abnormalities are seen in controls, it indicates the presence of CHD which had not yet become clinically overt and that collateral circulation was not as abundant as in those patients with normal records. A nine year follow up study to test this hypothesis has now been completed by Baker³ and indicates that the BCG wave form has impressive power to predict the development of CHD.

A normal control group of 265 men and women divided equally by decades were carefully studied and the BCG were classified as normal or abnormal on the basis of wave form inspection. The controls whose BCG's were abnormal at the outset developed events attributable to coronary artery obstruction five to six times as frequently as did those with normal BCG's. There were over 300 patients with well documented evidence of CHD and they too could be similarly subdivided on the basis of BCG wave forms. Those with abnormal wave forms developed twice the number of recurrences than did those with normal ones. Using the multivariate logistic function, the data indicated that the risk of development of CHD in the control group is strongly dependent upon age, but equally strongly and independently dependent upon the wave form of the BCG.

When one studies a third group of control subjects with a minor abnormality in blood pressure, heart size or even in all three, the BCG wave form retains its rank as a superior predictor of events. The BCG wave form predicts the likelihood of recurrence of an event in those who entered the study as patients with CHD significantly, but less impressively than it did with initial events in the control group. The conspicuous age dependence of initial events found to be characteristic of the controls is absent in the patients. The singular fact is that once the manifestations of CHD have appeared, the wave form of the BCG provides strong evidence of the likelihood of recurrences regardless of the age of the patient.

One can say from Starr's and Baker's studies and from Deuchar's⁴ as well, that the BCG provides a kind of information fundamentally related to the

appearance or recurrence of myocardial ischemia. These are extremely interesting studies. One cannot yet say precisely that the BCG's recording hemodynamically on man is what accounts for this predictive power. There remain several questions which progress to date has not answered. A better method for quantitating records of bizarre wave forms would serve to improve their interpretation. Much more needs to be done to improve our knowledge of the relation of the BCG abnormality and simultaneously recorded hemodynamic variables in man. To date all prospective studies have been based upon resting records. It is obvious that much more information would result from records which record the response to various stress procedures such as physical exercise.

Now that reliable BCG beds are commercially available, doubtless many new observers will seek to utilize the important predictive information obtainable from the BCG wave form.

L.H.N.

References

1. Starr, Isaac and Noordergraph, Abraham: *Ballistocardiography*. Philadelphia, J. B. Lippincott Co., 1967.
2. Starr, Isaac: Prognostic value of ballistocardiograms. *JAMA*, 187: 511, 1964.
3. Baker, B. M.: *Ballistocardiography: predictor of coronary heart disease*. *Circulation*, 37: 1, 1968.
4. Deuchar, D. C.: *Ballistocardiography*. *Brit. Heart J.*, 29: 285, 1967.

The Physician's Relation To The Trial Process

The physician may become involved in litigation as a dependent sued by a patient for malpractice. He may also be summoned into court as a witness as a result of his having treated a patient who has suffered personal injury as for example in an auto accident. In such a case he is asked to state what he observed of the patient's condition, his diagnosis and the course of his treatment. Lastly, he may be called to court as an expert witness and asked to give an opinion based on reasonable medical certainty of the cause of an injury. In this last capacity the "expert" physician may either have treated the patient or he may have been engaged by the other party to examine the patient or his records and render an expert opinion in court.

One of the most important phases of any case is the pretrial period termed "discovery". It is the time before trial during which a lawyer tries to find out as much as possible about his adversary's case and naturally the contents of the opponents medi-

cal testimony is a highly sought prize. The majority of the states allow very broad pretrial discovery, while other states allow very little about his opponents case. Under this limited discovery which exists in Connecticut the physician sued for malpractice would receive a maximum of thirty written questions from the plaintiff's attorney. He would then meet with his own attorney at his convenience and his answers to these questions or interrogations, needless to say would be noted for their brevity and lack of information.

In Connecticut either party can take the deposition of a physician who lives out of state or is going to sea or out of state or by reason of age or infirmity is unable to go to court or is over sixty years old. If the physician is in the state and available his deposition is not admissible unless both sides consent.² The Federal law as to the taking of deposition is much broader allowing either party to take the deposition of any witness. However, the deposition also is admissible only under restrictive circumstances such as living more than 100 miles from the place of the trial or out of the United States unless the party offering the deposition procured the absence or is unable to attend due to age, sickness, infirmity or imprisonment, not amenable to subpoena; or under exceptional circumstances which are undefined.

In Massachusetts, on April 1, 1966,³ a radical change was made from limited to broad pretrial discovery, or "oral discovery." The effects of this change are now just beginning to be felt. The differences for the physician are profound. Under Rule 15, the new Massachusetts discovery procedure, the dependent doctor can be summoned to the opposing attorney's office to undergo a process known as deposition (unlimited oral questioning). The plaintiff's lawyer chooses the time and place of the deposition and can ask the physician as many questions as he wishes for as long as he wishes about what occurred during the operation, in procedure alleged to have caused the injury.

Under present Connecticut and former Massachusetts rule the physician who would be summoned at the time of trial as an ordinary witness because he treated an injured accident victim, he could not be asked any questions written or otherwise. Under the new oral discovery rule in Massachusetts he too can be summoned to the opposing attorney office and questioned orally for as long as the attorney wishes.

The purpose of the broadened discovery clearly is to encourage settlement and reduce the element

of surprise. We are told by Chayet³ that the oral discovery procedure has now been used extensively in malpractice cases and has resulted in settlement before trial when facts that support the plaintiff's claim are brought out. This saves the embarrassment and expense of a jury trial which could end in a more costly verdict. The procedure could and actually has resulted in discontinuance of actions against physicians when the deposition reveals a case without merit.

One result of the deposition taken of a treating physician has often been that plaintiff and defense lawyers agree to use the deposition at the time of trial instead of requiring the physician to testify, again, saving a great deal of his time. The deposition is always a more efficient time saving procedure, occurring at a definite time and place as opposed to a trial where much of the treating physician's time may be spent in the courtroom while he waits to testify. The deposition is recorded by a court stenographer and direct examination as well as cross-examination takes place although no judge is present. Furthermore, attorneys usually attempt to choose a deposition time that will be convenient for the doctor. Experience thus far reveals that abuse of the deposition privilege has rarely occurred.

The physician who receives a deposition notice is supposed to immediately get in touch with his attorney or the attorney representing the patient. Promptly informing the opposing attorney if the time is inconvenient usually results in an appropriate change. Failure to be present at the time of deposition could result in a penalty for contempt of court. Attorneys, however, are generally very cooperative with the physician in this regard. What may stand in the way of liberalizing the rule on "oral" discovery in Connecticut is the position of many attorneys who prefer to have the doctor on their side testify in person as it may lend impact and drama to the doctor's words.

One of the most interesting questions is whether a deposition can be taken of an expert witness whose function is to give opinion testimony as opposed to the treating physician or one sued for malpractice, who is asked to state what he observed or what he did. The expert medical witness who appears at trial is usually retained at a substantial cost to the client. The opposing attorney should not be able to get the benefit of this opinion at no cost.

This problem is not resolved by Rule 15 in Massachusetts but cases that have been interpreted,

have rested upon federal rules which state that under no circumstances can the attorneys expert be questioned before trial. Chayet quotes such a case involving a death action in which a physician was employed by the plaintiff to render an opinion of whether the injury inflicted by the defendant caused the death in question. The defendant tried to take the deposition of the physician and thus find out his opinion without payment of any fee. The court stated "there is a distinction between the case of a man who sees a fact and is called upon to prove it in a court of justice, and that of a man who is selected by a party to give his opinion on a matter with which he is peculiarly conversant . . . the former is bound as a matter of public duty to speak to a fact which happens to have fallen within his knowledge . . . The latter is under no such obligation." *Boynton, V. R. J. Reynolds Tobacco Co.*, 36 F. Supp. 593 (1941).

In Massachusetts oral discovery is clearly here to stay. If used with discretion by the attorney and understood by the physician it can be a forward step in the efficient disposition of difficult litigation. It's time Connecticut introduced similar legislation to Massachusetts Rule 15 on "oral" discovery.

L.H.N.

References

1. Mitchell Fenton. Personal Communication.
2. Conn. Statutes 52-148 et seq and Rule 26 of Federal Civil Procedure.
3. Chayet, N. L.: *Law Medicine Notes: The Physician and Oral Discovery*. *New Eng. J. Med.*, 277: 752, Oct. 5, 1967.

Insulin Resistance And Diabetes Mellitus

The basic nature of human genetic diabetes mellitus remains a mystery. Considered thus far as possible defects are an abnormal or insensitive regulatory mechanism for insulin secretion, an abnormal form of insulin and some type of insulin antagonism.¹ These hypotheses have developed because we have learned a great deal about diabetes, but the difficulty of understanding it arises mainly in the effort to decide which abnormality is the primary pathologic process, the direct reflection of the damaged gene and which are the indirect secondary aspects.

The common mechanism for all diabetic states appear to be insufficient insulin. One extreme is the absolute lack of insulin when the pancreas is ablated. At the other extreme is the massive insulin secretion in the patient with a great enough degree

of insulin secretion yet suffering from a relative insulin lack. A well studied example of experimental insulin resistance and relative insulin lack is the dog who has received sufficient quantities of growth hormone. An illustration of the human response to insulin resistance is afforded in acromegaly. The degree of insulin resistance does not differ quantitatively between diabetic and non-diabetic acromegalic subjects. The insulin output is very great both in the normoglycemic and hyperglycemic acromegalic. If one removes excess of the growth hormone in acromegalics then alterations due to insulin resistance is completely reversed and insulin secretion becomes normal.¹

There is thus a triad of resistance to insulin, compensating increase in secretion of endogenous insulin, and reversal of insulin resistance on removal of the offending "factor". It occurs in other physiologic states besides acromegaly such as pregnancy, obesity, corticosteroid therapy and pathologic corticosteroid excess as in Cushing's syndrome. But not every acromegalic develops diabetes. It must be that the acromegalic diabetic though he releases greater than normal quantities of insulin, still shows relative insulin lack.

One important question raised by insulin resistance is the mechanism whereby the beta-cells sense the insulin resistance and start to compensate. It is possible that no matter what the specific etiology of insulin resistance is, the need for more insulin is signaled to the pancreas through some common metabolic indicator such as the mean daily level of blood sugar. One can by prolonged glucose infusion at a rate that increases the mean blood sugar only slightly, increase the subsequent beta-cell response. There is also evidence that at least some humoral factors such as growth hormone may also have a direct "trophic" effect on the beta-cells. This idea is supported by increased beta-cell responsiveness when one injects growth hormone and this precedes detectable alterations in the daily mean blood glucose levels.

Another question is why it is that the beta-cells fail to meet the challenge of insulin resistance in those diabetic patients who are insulin resistant. It appears that the percentage of patients with Cushing's or acromegaly in whom overt diabetes develops closely approaches the suspected gene frequency for diabetes in the population at large, that is about 20-30 per cent of the total group. It has been suggested, therefore, that in insulin-resistant states a relative beta-cell failure results from the presence of the gene for diabetes which ex-

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presses itself by preventing the beta-cell from responding adequately to the blood glucose stimulus.

We may then say that the normal pancreas appears capable of prodigious feats of insulin secretion in response to insulin-resistant stresses. Nevertheless sheer exhaustion of the pancreas does not appear to be an important mechanism in the development of overt diabetes in insulin-resistant states such as acromegaly. Diabetes becomes clinically manifest only through a diminution in the response of the beta-cells to a given stimulus and this diminution may be genetically determined.²

One is led to conclude that prolonged insulin resistance by itself may not induce or even hasten the rate of progress of genetically determined beta-cell dysfunction. It may only make more apparent the natural progression of this beta-cell dysfunction.

L.H.N.

References

1. Davidoff, F. F.: Oral hypoglycemic agents and the mechanism of diabetes mellitus. *New Eng. J. Med.*, 278: 148, Jan. 18, 1968.
2. Graber, A. L., Wood, F. C. and Williams, R. H.: Serum immuno-reactive insulin response during prolonged glucose infusions in non-diabetic and diabetic humans. *Diabetes*, 16: 145, 1967.

About Human Variety—Studies On Genetic Variations

In his catalogue of Mendelian characteristics of man¹ McKusick lists 1,545 genetically determined variations indicating the existence of mutant genes of at least that many loci. Most of the hereditary variations listed are diseases usually rare and often involving many organ systems. In only 15-20 per cent has a relation between a given gene and some particular metabolic function been identified. In even fewer perhaps 5 per cent is information available to indicate either the quality or the rate of synthesis of specific protein has been altered. The catalogue gives some information concerning the extent of heterogeneity of genes at many of the loci examined and it becomes evident that each locus may be occupied by more than one or even many alternative genes (that is alleles).²

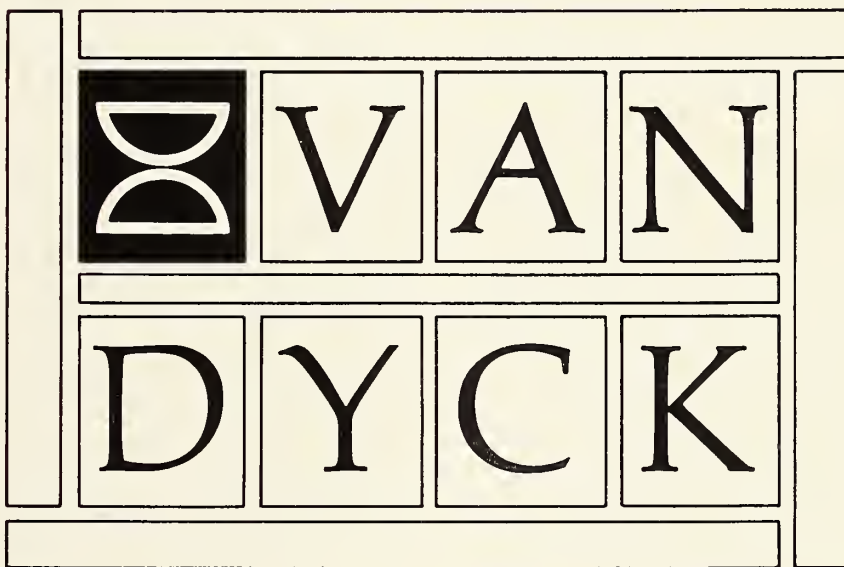
The human geneticist thus has several tasks: to identify additional loci showing variations to discover how many alleles there are at each locus, and to relate each allele to the phenotypic nuance that it governs. The microbial geneticists have taught us that genes act by specifying the sequence of aminoacids in proteins and by controlling the rate

of protein synthesis in response to the metabolic requirements of the cell. Mutational events occurring at the time of replication of DNA are reflected in changes in the arrangement of aminoacids in the proteins or in alterations of the rates and times of their formation. Such mutations result in much genetic and consequently phenotypic heterogeneity.

Knowledge of the nature of mutagenesis is now of increasing importance because a study of the properties of many proteins has revealed an unexpectedly abundant and frequent degree of variation. Childs and Der Kaloustian³ now document in detail the recent accumulation of evidence for hereditary biochemical variation in man and emphasize the importance of this subject for our understanding of the inheritance of normal and abnormal traits. The variations result from the substitution of one aminoacid for another in a structuring or an enzymatic protein which is caused by a mutation in the gene for that molecule. Such substitutions can probably occur in any position in the polypeptide chain even though present methods are inadequate to detect them all. We do not know why certain substitutions occur more frequently than others. Some alter the molecule but slightly. However, should one directly or indirectly affect the biological activity of the protein markedly it will cause disease.

A variety of forms of most proteins probably exist in the human population ranging from "normal" to totally inactive molecules and these are reflected in clinical spectrums from health to full blown disease. A substitution that does not result in complete loss of enzymatic activity will change the clinical picture. For example total loss of guanine hypoxanthine phosphor ribosyl transferase causes the rare hyperuricemia oligophrenia syndrome whereas partial loss leads to gout.⁴ Further heterogeneity in some rare recessive disorders arise from the fact that the affected homozyote is actually more likely to have two identical mutations at his two homologous loci. The last point of great interest is that abnormalities in different enzymes can at times produce the same clinical picture as in hyperphenylalaninemia⁵ or the congenital nonspherocytic hemolytic anemia.⁶ Clearly optimal therapy will eventually have to be guided by knowledge of the precise molecular lesion, a somewhat discouraging outlook.

The method used to detect the variations of the thirty-eight protein types described, consisted of electrophoresis in twenty-eight, by immunologic means in eight, by tests of stability after heating in



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one and by differential response to an enzyme inhibitor in one. After discovery the variant molecules are usually tested for other attributes such as stability to heat, biologic affinity for substrates, pH, optimum response to inhibitory substances or immunologic change. Once the protein is purified, the variants are analyzed for sequence of their component aminoacids.

Some proteins were identified in the course of studies of hereditary diseases while other were discovered as by products of research done for reasons having nothing to do with genetic variability. Recognition of many of the more recent variants is a result of a purposeful search for molecular variation. Among human proteins the hemoglobins have been subjected to the most extensive analysis. In all there must be more than 150 hemoglobins reported. The vast majority of the variants involve substitution of one aminoacid for another, but there are also two deletions listed and one molecule that represents a fusion product of beta and delta chains. This indicates that not all variations result from point mutations.

There are many aminoacid substitutions that leave the molecule functionally intact whereas others in different parts of the molecule are injurious. The amount of variations that are rapidly becoming apparent is constantly increasing. The combinations of the particular products of the genes of a human being present in particular amounts and appearing at particular times in development are the fabric of his individuality. It is the sum of the action of all the genes functioning in a cell at a given moment that provides the metabolic climate of the cell.

Perhaps of great importance is the role of subtle modifications of proteins acting together in the inheritance of traits that do not behave as single genes. Through further studies on genetic variations we may begin to understand characteristics that are "multifactorial" and continuously distributed such as intelligence and height, the molecular meaning of "low penetrance" and "variable expressivity," the obscure inheritance propensities to infection and common ailments such as allergy and hypertension. Because of the multitude of proteins and each variable that would interact to determine these traits, it might require large computers to bring these into some form of synthesis.⁷

L.H.N.

References

1. McKusick, V. A.: Mendelian inheritance in man. Second edition, Johns Hopkins Press, Baltimore, 1968.

2. Harris, H.: "Inborn errors" today. In Garrod's inborn errors of metabolism. London, Oxford, 1963, p. 183.
3. Childs, B. and Der Kaloustian, V. M.: Genetic heterogeneity. *New Eng. J. Med.*, 279: 1205, 1968.
4. Kelley, W. N., Rosenbloom, F. M., Henderson, J. F. and Seegmiller, J. E.: Specific enzyme defect in gout associated with over production of uric acid. *Pro. Nat. Acad. Sci.*, 57: 1735, 1967.
5. Carpenter, G. G., Auerbach, V. H. and George, A. M.: Phenylalaninemia. *Ped. Clin. North America*, 13: 313, 1968.
6. Hereditary disorders of erythrocyte metabolism. Ed. by E. Bentler, New York. Grune, 1967.
7. Neel, J. V. and Schull, W. J.: On some trends in understanding genetics of man. *Perspec. Biol. and Med.*, 11: 565, 1968.

Medical Dogma: The Duration Of Pregnancy

When we talk about the length of pregnancy we should mean from conception to delivery. The accepted method of calculation of the expected date of delivery (EDD) is found in all text-books. Ask for the date of the last menstrual period (L.M.P.) add seven days and subtract three calendar months. For example if the L.M.P. was on June 5, 1968 then the EDD would be March 12, 1969. Whichever date in the year is taken the interval between L.M.P. and EDD comes out approximately 40 weeks or 280 days. The way this method of calculation came into vogue many years ago was because it was believed that conception was most frequent during the week after the end of menstruation. This idea, however, was rejected when it was realized that orthodox Jewish women who are barred from intercourse during this period were extremely fertile nevertheless.

It is now accepted that ovulation most frequently happens on about the 14th day of the menstrual cycle. After stating this, the typical obstetrical text-book goes on to say "since there is no definite means of knowing the time at which conception occurs it is usual and convenient to calculate the date on which delivery is to be expected from the first day of the last menstrual period.¹ In this case we include a week when pregnancy is quite unlikely and a week when it is almost impossible. Therefore no matter how usual or convenient the other definition is there is no doubt it is false. This error continues to be perpetuated in our teaching. We talk about a woman being 20 week pregnant when it is really 18 weeks.

For a number of years Dalton has taken accurate notes of details of every pregnancy in her general practice amounting to 2,100 in women who were reasonably accurate in their dates and only

pregnancies which ended spontaneously and resulted in a normal birth were included in her analysis. The peak period turned out to be at the end of the 41st week and the beginning of the 42nd, that is 7th, 8th, and 9th day after EDD. These figures correspond very closely to those in a chapter on post-maturity² which states that based on a large number of cases, a case can easily be made showing that one-fourth of cases of pregnancy will be delivered during the 42nd week, 12 per cent during 43rd week and 3 per cent during 44th week after the beginning of the last period but in any particular pregnancy the diagnosis of post-maturity is usually uncertain."

The majority of normal births, that is 57 per cent take place in the 41st and 42nd week but despite the good advice given in this text-book, it seems to be common practice to induce labor during this period to avoid delivery of too large a baby. It would seem that this is often done because of unnecessary anxiety about the time factor in the mind of the mother. Dalton, however, considers the 41st, 42nd and 43rd weeks as period of non-intervention unless there is good reason. She points out that the benefits arising from this policy has payed-off in significantly low perinatal mortality (4 per 1,000 births).

She wonders whether the old method of calculation of pregnancy may not have contributed unnecessarily of interfering "with the very wonderful natural processes of childbirth. In her view it would be convenient and infinitely more consistent with what we know about the time of ovulation if we would calculate the EDD by taking the first day of L.M.P. and adding fourteen instead of seven days. This would mean 41 weeks after the first day of the last period and would also mean approximately 39 weeks of conception. It would also prevent much confusion if we referred to term as approximately 39 weeks so that when we say 39 weeks we really mean it.

L.H.N.

References

1. Park, G. L.: The duration of pregnancy. *Lancet*, II: 1388, December 28, 1968.
2. Clayton, S. G., Fraser, D. and Lewis T. L., T. (Editors) *Obstetrics by Ten Teachers*. London, 1960.

How Well Does The Transplanted Kidney Perform

Certain death faced the patients with terminal renal failure until recently when refinements in surgical techniques and improvement in immuno

suppressive therapy opened new hope with kidney transplantation. Successful homotransplantation of the kidney between live related donors may be achieved in about half the cases. Cadaver transplants may approach this success rate also and some recipients of renal allografts are reported to be alive and well more than three years after operation.

There are problems introduced by transplantation that have to be recognized. The transplanted kidney has been denervated, turned over in its side, has lost its lymphatic return and except in the case of the identical twin is probably subjected also to repeated immunologic insults. Ultimate success then clearly depends not merely on expert surgical technique and overcoming immunologic mechanisms, but also on how well the kidney functions physiologically.

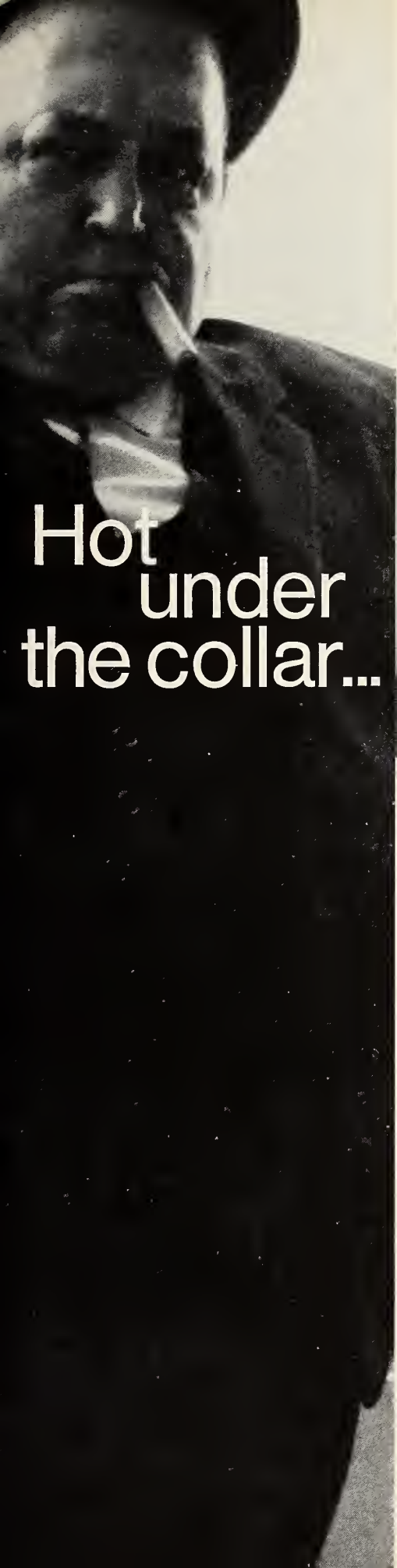
"The kidney" stated Homer Smith "is the organ par excellence of evolution." Throughout phylogenetic history this organ has an astonishing adaptability in defending the constancy of the internal environment in the entire vertebrate class.

The transplanted human kidney is expected to respond to physiologic stimuli of its new host and begin at once to regulate and defend the alien milieu. How well does it do this? Fortunately it is possible to study how well it performs its function under new circumstances. Blaurock et al¹ have now documented that the new kidney meets its challenge ably at least under favorable circumstances. Their data on sodium and creatinine clearance on five homotransplanted and one isograft (identical twin) donor and recipient pairs show little or no difference in glomerular filtration rate and renal plasma flow between the paired kidneys whether they function in the donor or recipient.

These findings confirm those already reported by Ogden^{2, 3} who found only slight differences in these functions. After nephrectomy in normal animals and man, rapid functional hypertrophy of the remaining organ ensues which soon is able to perform 70 per cent of the activity previously exhibited by both organs. Anatomic enlargement of the organ follows later. Clearly if the donor and recipient kidneys perform identical functions, then it follows that the transplanted organ not only has held its own but has also hypertrophied like its mate. From Parker et al's⁴ studies there is evidence of structural as well as functional hypertrophy.

In addition to preservation of filtration rate and renal plasma flow, the transplanted organ retains its ability to respond promptly and normally to





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Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs.

Use in pregnancy: Because chlorthalidone may cross the placental barrier and appear in cord blood and thiazides may appear in breast milk, this drug should be used with care in pregnant patients and nursing mothers. When used in women of childbearing age, the potential benefits of the drug should be weighed against the possible hazards to the fetus. Use of chlorthalidone may result in fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to

reserpine-treated mothers.

Precautions: Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, the drug should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Severe salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute

gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angitis are possible.

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changes in sodium intake by saving or excreting sodium as needed. There occurs also a normal release of renin in response to the stimulus of a low sodium intake. With normal renin release, the resulting aldosterone production is not impaired. Studies such as this¹ nicely demonstrate the precision of the kidney humoral auto regulatory mechanism and its independence from nervous system control.

Bricker et al⁵ in a study on identical twin transplant recipient and his donor showed that the denervated kidney can regulate electrolyte excretion, respond normally to vasopressin, regulate fluid volume and function normally in most respects. However, the phenomenon of rejection does not occur here. Rejection is essentially a disorder of the interstitium and of the renal vasculature at first. Later the glomerular changes occur as well. Under these conditions permanent abnormalities of renal perfusion, urinary concentrating ability, renal tubular and glomerular filtration, might occur in the homograft which demonstrates both reversible and irreversible renal change as a result of rejection.

In view of the paucity of identical twins and the necessity for homografts the question remains whether renal homotransplantation should now be regarded as an experiment or therapeutic procedure. Studies of the function of transplanted kidneys, among patients who are doing well as in Blaufox's cases really do not bear on this question. The major problems in the area of renal transplantation are still immunologically induced renal damage with impairment of renal functions and sepsis. Somewhere in the process the problem of destruction of lymphatic drainage has been lost sight of and what role this plays in the 50 per cent failures mentioned above. As an experiment kidney transplantation should be encouraged. As a treatment it is still debatable. This is one reason why surgeons are depending more on cadaver kidneys and less on kidneys from live donors.⁶

L.H.N.

References

1. Blaufox, M. D., Lewis, E. J., Jagger, P., Lauler, D., Hickler, R. and Merrill, J. P.: Sodium regulation and renin secretion by transplanted human kidneys. *New Eng. J. Med.*, 280: 62, Jan, 9, 1969.
2. Ogden, D. A.: Donor and recipient function 2-4 years after renal transplantation. *Ann. Int. Med.*, 67: 998, 1967.
3. Krohn, A. G., Ogden, D. A. and Holmes, J. H.: Renal function in 29 healthy adults before and after nephrectomy. *JAMA*, 196: 322, 1966.
4. Porter, K. A., Marchioro, T. L. and Starzl, T. E.: Pathological changes in 37 human renal homotransplants

treated with immunosuppressive drugs. *Brit. J. Urol.*, 37: 250, 1965.

5. Bricker, N. S., Guild, W. R., Reardon, J. and Merrill, J. P.: Studies on functional capacity of denervated homotransplanted kidney in identical twin with parallel observations in donor. *J. Clin. Investigation*, 35: 1364, 1956.

6. Nahum, L. H.: Medical and ethical aspects of kidney transplantation. *Conn. Med.*, 32: 562, August 1968.

Who Reports On Interaction Of Nutrition And Infection

It is perhaps common knowledge that a malnourished person is unusually susceptible to disease and that infectious diseases can in turn influence the nutritional status. An example is kwashiorkor which is precipitated by infection in children who are protein deficient. The details of the complex interaction between nutrition and infection are however less well known. Ordinarily in man the interactions are regularly synergistic. Malnutrition and infection are mutually aggravating and produce more serious consequences than would be expected if the independent effects of the two were merely additive. However, a reverse antagonistic effect may also occur when highly specific deficiencies inhibit the multiplication of the infectious agent more than the resistance of the host.

Probably the first indication of poor nourishment favoring resistance is the observation of Peyton Rous in 1911 that healthy well-nourished chicks were more susceptible to the fowl sarcoma virus than those which were undernourished. Then came similar results with fasting and well-fed rabbits in relation to vaccinia virus. It is now definitely established that in a number of cases of deficiency of particular nutritional essentials may increase natural resistance. This phenomenon of increased natural resistance due to a deficiency is not limited alone to viruses. Riboflavin deficiency in chickens increases resistance to avian malaria.

In general, however, bacterial, viral protozoal and helminthic infections all exert a detectable adverse effect on nitrogen balance. Keratomalacia, scurvy and beri-beri are frequent aftermaths of an infectious process in people subsisting respectively on diets deficient in vitamin A, ascorbic acid and thiamine and in fact there has accumulated a large body of evidence confirming the adverse effect of infection on the metabolism of these vitamins. Infections also interfere with the metabolism of calcium and phosphorus. Chronic infections alter iron metabolism and erythrocyte production to such an extent to permit the development of the so called "anemia of infection."

Severe deficiencies of ascorbic acid and B complex vitamins definitely lower resistance of man to most infectious diseases. The idea that adding these substances to adequate diets in these vitamins will increase resistance to infection is however not borne out by experiments. Malnutrition apparently lowers host resistance by interfering with antibody formation, phagocytic activity, endocrine metabolism and non-specific protective mechanisms. Protein deficiency especially inhibits normal antibody response and there is abundant evidence that vitamin deficiencies can have the same effect. Vitamin B complex deficiencies also reduce white blood cell activity and decreased macrophage activity has been also associated with deficiencies of vitamin A and ascorbic acid.

Another effect of malnutrition is an alteration in the types, number and distribution in intestinal bacteria and this may bring about decreased resistance to intestinal infections. Under special conditions dietary imbalance alters the therapeutic effectiveness of a number of drugs. For example *plasmodium gallinaceum* infection of chicks responded 4-20 times more readily to treatment with sulphadiazine or metachloridine when the birds were on a purified casein diet rather than on a regular stock diet. However, this accentuated treatment effect was later diminished when an increased amount of soy bean was added to the diet.

In most cases antagonistic interaction between a nutritional deficiency and an infection seem to be caused by a selective lack of one or more nutrients on which the infectious agent is more dependent than is the host.

L.H.N.

References

- Disease and diet. *Nature*, 221: 304, Jan. 25, 1969.
Modern nutrition in health and disease. Michael G. Wohl and Robert S. Goodhart. Lea & Febiger, Philadelphia, 1960.

Attack On German Measles

Ten to twenty thousand malformed infants resulted following a rubella epidemic in this country 1963-1964.¹ Now Parkman et al² have developed an attenuated rubella virus vaccine by 77 serial passages of the virus through African green monkey kidney cell culture. Trials on monkeys and in children demonstrated that the strain used could when inoculated subcutaneously induce antibody formation. Such individuals did not develop rubella during an epidemic of the disease. It was then tried on over 3,000 young people in Taiwan.³ The percentage efficiency in preventing rubella with rash is 93-

94 per cent after three weeks as compared with a control group. Three anaphylactic reactions 5-10 minutes after injections occurred following the use of a DK vaccine. The three responded well within 1-2 minutes after receiving epinephrin subcutaneously. The DK vaccine was accordingly discontinued.

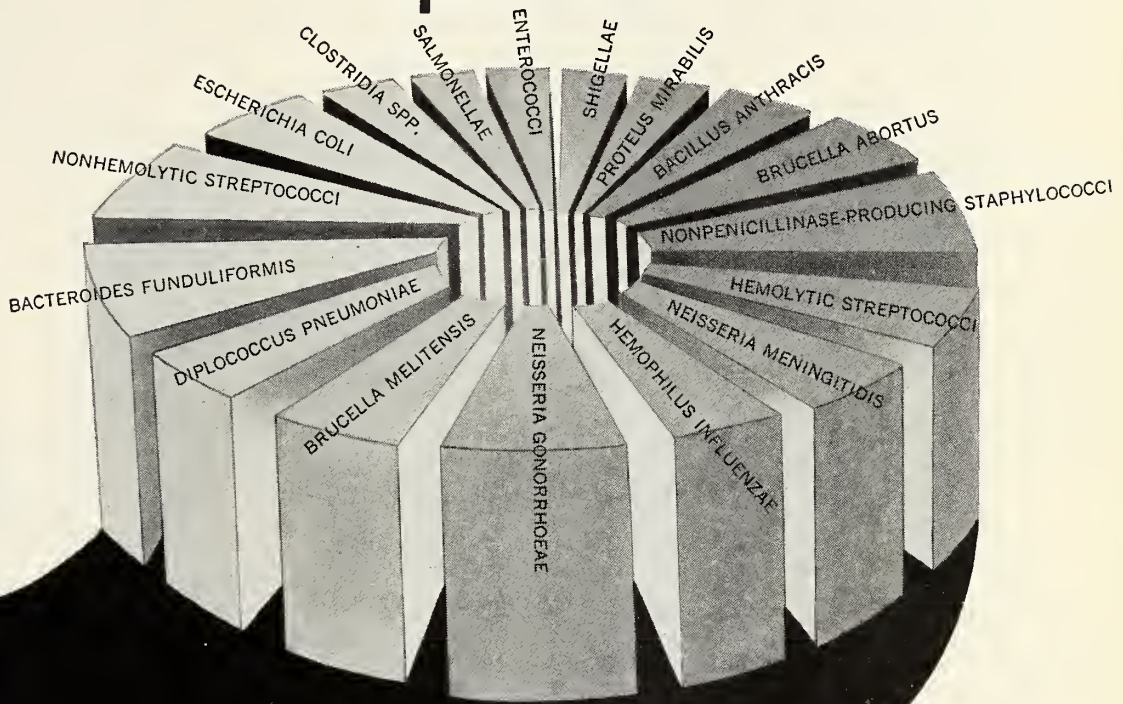
Live vaccines often have a protective effect even prior to the development of measureable antibodies. The onset of protection develops 2-3 weeks after the injection. Thus if the wild virus invades the body at the time of injection of the vaccine, the course of the resulting infection is not altered. But if the vaccine virus has been injected a sufficient time prior to exposure to the natural virus there is prevention or modification of the infection. The clinical diagnosis of rubella may at times be difficult in sporadic cases. In an epidemic, however, the certainty of diagnosis is greatly increased. Other diseases may also cause a rash but this would not have the effect of increasing the calculated efficiency of the vaccine.

One question not yet answered by Grayston's study is whether the vaccine, like immunoglobulin modified rather than prevented the disease. Another important question which Grayston's trial does not answer is the length of protection following immunization with HPV-77 strain vaccines. Meyer and Parkman's⁴ study have shown persistence of antibody for two years.

Manufacturers are currently seeking approval for at least three rubella vaccines on which large scale field trials have already been done. Many reports at the International Conference on Rubella Immunization in Bethesda, Maryland noted the efficacy and safety of all three. Once the vaccines are licensed the U.S. Public Health Service will launch a major campaign to immunize children against rubella in an effort to eradicate the disease in this country. It is probable also that women in the child bearing age who are not pregnant at the time and are not likely to become pregnant within a month will also be given the vaccine. Obviously it would be dangerous to give the virus vaccine to a pregnant woman because it is not known whether the virus would affect the fetus.

European doctors are also considering giving the vaccine to women who have just completed a pregnancy on the ground that they are assuredly not pregnant at the time of vaccination and that the vaccine will protect them for future pregnancies. This method however has not been settled as a procedure in this country.

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Contraindications: A history of allergic reactions to penicillins or cephalosporins and infections due to penicillinase-producing organisms.
Precautions: Typical penicillin-allergic reactions may occur, especially in hypersensitive patients. Mycotic or bacterial superinfections may occur. Experience in newborn and premature infants is limited and caution should be used in treatment, with frequent organ function evaluations. Safety for use in pregnancy is not established. In gonorrheal therapy, serologic tests for syphilis should be performed initially and

monthly for 4 months. Assess renal, hepatic and hematopoietic function intermittently during long-term therapy.

Adverse Reactions: Skin rash, pruritus, urticaria, nausea, vomiting, diarrhea and anaphylactic reactions. Mild transient elevations of SGOT or SGPT have been noted. Black tongue has been noted in some patients receiving the Chewable Tablets.

Usual Dosage: Adults—250 or 500 mg. q. 6 h. (according to infection site and offending organisms). Children—50-100 mg./Kg./day in 3 to 4 divided doses (depending on infection site

and offending organisms). Bacterial meningitis—150-200 mg./Kg./day in 6 to 8 divided doses. Children weighing more than 20 Kg. should be given an adult dose when prescribing orally. In parenteral administration, children weighing more than 40 Kg. should be given an adult dose. Beta-hemolytic streptococcal infections should be treated for at least 10 days.

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L.H.N.

References

1. Horstman, D. M.: Rubella and the rubella syndrome: problems and progress. *Med. Clin. N. Amer.*, 51: 587, May 1967.
2. Parkman, P. D. et al: Attenuated rubella virus: I. Development and laboratory characterization. *New Eng. J. Med.*, 275: Sept. 15, 1966.
3. Grayston, J. T. et al: Field trial of live attenuated rubella virus vaccine during an epidemic on Taiwan. *JAMA*, 207: 1107, Feb. 10, 1969.
4. Meyer, H. M. et al: Clinical studies with experimental live rubella virus vaccine (Strain HPV-77). *Amer. J. Dis. Child.*, 115: 648, June 1968.

Surgical Treatment Of Coronary Artery Disease

When drugs and other medical measures fail to control severe angina pectoris, surgery is sometimes employed to reduce the frequency and severity of the pain by improving the blood supply to the heart. Although many surgical procedures have been tried in the past, the two most promising ones are direct implantation of an internal mammary artery into the myocardium, and coronary artery endarterectomy with or without patch grafting.

INDICATIONS FOR SURGERY—Surgery is usually limited to patients with intractable angina not relieved by drugs or other medical measures and who have angiographically demonstrated constriction of a major coronary vessel to less than 25 per cent of its normal diameter. It is believed that this degree of occlusion is necessary to encourage an implanted vessel to remain patent and establish collateral circulation within the myocardium. Some surgeons consider surgery inadvisable if there is complete absence of collateral flow from other main coronary vessels, as demonstrated by coronary cinearteriography (F. M. Sones, Jr. and E. K. Shirey, *Mod. Conc. Cardiovasc. Dis.*, 31:735, 1962).

INTERNAL MAMMARY ARTERY IMPLANT—The technique of implantation of an internal mammary artery first described by A. M. Vineberg (*Canad. Med. Ass. J.*, 55:117, 1946) has undergone many modifications, but the basic procedure of burying a systemic artery in the ventricular wall with its end closed and its side branches open is

usually followed. In a recent study (R. G. Favaloro et al., *Circulation*, 37:549, 1968), 150 patients were observed for 15 months or less after implantation of both internal mammary arteries into the myocardium. Fourteen of the patients died in the early postoperative period, usually of massive myocardial infarction; improvement of angina was reported in 116 of the 136 survivors. Postoperative angiographic studies on 31 of the patients who improved showed that in most of these patients there were patent internal mammary arteries and definite communication with a coronary artery.

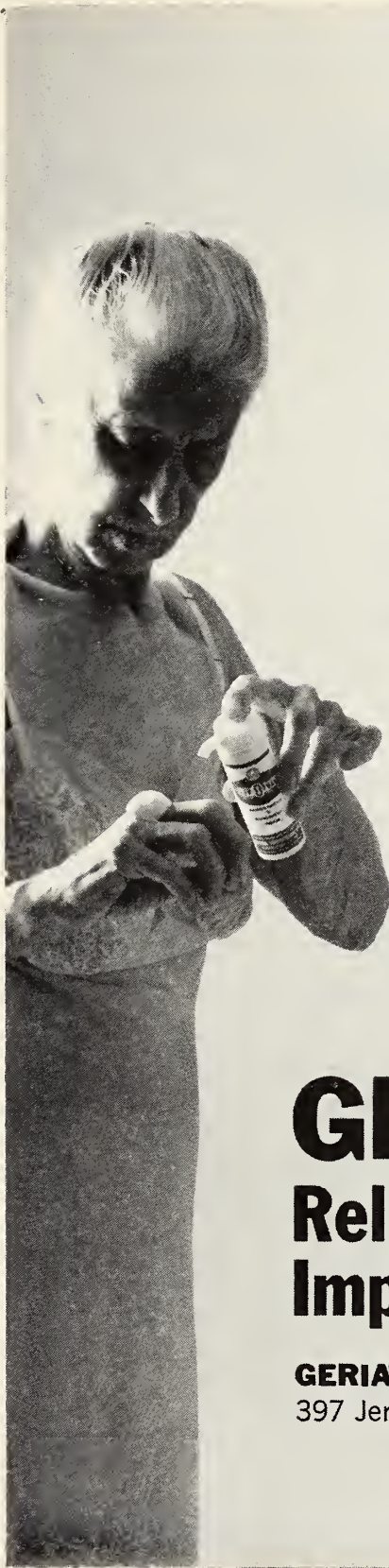
D. J. Fergusson et al. (*Circulation*, 37[Suppl. 2]:24, 1968) reported fair to excellent clinical improvement of angina in 66 per cent of 249 patients, most of whom were observed for three to four years after left internal mammary artery implantation. Postoperative arteriograms in 127 patients showed patent implants in 117 patients and communication with a coronary artery in 69.

R. Gorlin and W. J. Taylor (*New Eng. J. Med.*, 275:283, 1966) evaluated the postoperative results of internal mammary artery implantation by biochemical analysis of coronary sinus blood as a reflection of surgically altered myocardial metabolism. These investigators have demonstrated reversal of the preoperative myocardial lactate production in six of nine patients tested.

CORONARY ENDARTEROTOMY AND GRAFTING—D. B. Effler et al. (*J. Thorac. Cardiovasc. Surg.*, 53:93, 1967) performed coronary endarterectomy with transluminal dilatation above and below the sites of constriction in patients who had at least 75 per cent occlusion of a main coronary artery. The method gave initially good results in most patients with disease limited to the right main coronary artery. Results were less satisfactory in patients with obstruction of other coronary artery branches.

CONCLUSION—Internal mammary artery implantation and coronary endarterectomy with grafting are promising surgical procedures for controlling severe angina not responding to medical measures. In the absence of well-controlled trials comparing surgical procedures with medical management, however, some cardiologists believe that the benefits are due mainly to intensive postoperative medical care and exercise programs and to psychological factors rather than to improved coronary artery circulation.

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y. Vol. 11 No. 3 February 7, 1969.



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1. Gordon, E.E. and Haas, A., *Industr. Med. Surg.* 28:217, May, 1959.

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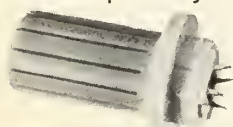
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MEETINGS

GENERAL

April 9

177th Annual Meeting, Hartford County Medical Association

Hartford Hilton Hotel

Business Meeting 5:00 P.M., Reception 6:45 P.M.,
Dinner 7:00 P.M. Speaker, Norman Cousins,
Editor, Saturday Review

April 15

177th Annual Meeting, Fairfield County Medical Association

Frederick's, Fairfield

Business Meeting 4:00 P.M., Dinner 7:00 P.M.

May 13, 14, 15

177th Annual Meeting, Connecticut State Medical Society

Hartford Hilton Hotel

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospital, New London

May 6 7:15 P.M.

The Peripheral Nerve and Neuromuscular Function and their Disorders; The Physiology and Anatomy of Epilepsy.

H. Richard Tyler, M.D., Assistant Professor of Neurology, Harvard Medical School.

May 20 7:15 P.M.

Parathormone—Thyrocalcitonin

Dorothea Hellman, M.D., Assistant Professor in Medicine and Pediatrics, Tufts Medical School

CANCER

Oncology

Sponsored by the Connecticut Division of the American Cancer Society and the Yale Medical School.

Speakers: Yale Medical School

Russ Home Conference Room, Griffin Hospital, Derby

April 1 8:00 A.M.-9:00 A.M.

Management of Patients with Lymphoma

Ronald DeConti, M.D., Assistant Professor of Medicine and Pharmacology

Chairmen: Dr. DeConti; Vincent A. DeLuca Jr., M.D., Assistant Clinical Professor of Medicine

Open to all Physicians

May 8-10

National Conference on Breast Cancer

Shoreham Hotel, Washington D.C.

A multidisciplinary review of the breast problem in the U.S. will be presented, including epidemiology, etiology, detection, diagnosis, management and control measures.

Sponsored by the American Cancer Society and Cancer Control Program, U.S. Public Health Service

No fee; preregistration required

MEDICINE

Wednesdays 12:00 P.M.-1:15 P.M.

Pulmonary Diseases and Pulmonary Physiology

Radiation Center Conference, Room, Hospital of St. Raphael, New Haven

Chairman: John B. Berte, M.D., Director, Department of Pulmonary Diseases and Inhalation Therapy, Hospital of St. Raphael

Open to all physicians

Thursdays 1:30 P.M.-3:30 P.M.

Hematology

Hematology Laboratory and Wards, Hospital of St. Raphael, New Haven

Robert P. Zanes, Jr., M.D., Hospital of St. Raphael
Open to all physicians

May 15-17

Fifth Annual Cardiovascular Symposium

St. Francis Hospital, Hartford

Program: Advances in the Diagnosis and Treatment of Arrhythmias, Howard B. Burchell, M.D., Editor, "Circulation," Professor of Medicine, University of Minnesota Medical School; Present Status of Valvular Homografts and Heterografts, James R. Malm, M.D., Associate Professor of Surgery, Columbia University College of Physicians and Surgeons; Pathology of Coronary Artery Disease and Its Complications, Jesse E. Edwards, M.D., Clinical Professor of Pathology, University of Minnesota Medical School; Secrets in the Shadows—A Clinician's View of Cardiovascular Radiology, Joseph K. Perloff, M.D., Associate Professor of Medicine, Georgetown University; Cardiac Auscultation in Acquired Heart Disease, Bernard L. Segal, M.D., Clinical Associate Professor of Medicine, Hahneman Medical College;

PEDIATRICS

May 21

Scientific session sponsored by the New England Pediatric Society and New Haven Area Rehabilitation Center

Speakers: Yale Medical School, Viral Infections in Pregnancy as a Cause of Fetal Damage, Dorothy Horstman, M.D., Professor of Epidemiology and Pediatrics; The Effects of Maternal Analgesic Agents on the Fetal Heart Rate, Edward Hon, M.D., Associate Professor Obstetrics and Gynecology; Recognition of Minimal Brain Damage in Early Infancy, Sally Provence, M.D., Professor of Pediatrics; Minimal Brain Damage-Conceptions and Misconceptions, Ethelyn Klatskin, M.D., Assistant Professor Of Psychology; Behavior of the 'Brain Damaged' Child; John Schowalter, M.D., Assistant Professor of Pediatrics and Psychiatry. Early Educational needs of the Deaf Child, David Green.

Acute Pericarditis, David H. Spodick, M.D., Assistant Professor of Medicine Tufts University Medical School; Viral Diseases of the Values and Heart, Papillary Muscle Syndrome, George E. Burch, M.D., Editor, American Heart Journal, Professor and Chairman, Department of Medicine, Tulane University Medical School, Surgical Indications in Congenital Heart Disease, Alexander S. Nadas, M.D., Clinical Professor of Pediatrics, Harvard Medical School.

May 24

Eighth Annual Advanced Contact Lens Seminar

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Discussion: Soft lenses and aphakia; methods of fitting keratoconus, corneal grafts, astigmats and children

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177TH ANNUAL MEETING, HARTFORD HILTON HOTEL, HARTFORD, MAY 13-14-15 - 1969 EXHIBITS

<i>Space</i>	<i>Firm</i>	<i>Location</i>
1	William H. Rorer, Inc.	Fort Washington, Pa.
2	Silver Hill Foundation	New Canaan, Conn.
3	Dictaphone Corp.	Rye, New York
4	American Medical Building Guild	Madison, Wis.
5	Arthur W. Eade Insurance Agency	Hamden, Conn.
6	Surgeons & Physicians Supply Co.	Boston, Mass.
7	Mikelk Electronics	Auburn, Mass.
8	Eli Lilly and Company	Indianapolis, Ind.
9	Cameron-Miller Surgical Instruments Co.	Chicago, Ill.
10	D. G. Stoughton Company	West Hartford, Conn.
11	Syntex Laboratories, Inc.	Palo Alto, Calif.
12	Parke, Davis & Company	Detroit, Mich.
13	E. R. Squibb & Sons	New York, N.Y.
14	Medical Plastics Laboratory, Inc.	Gatesville, Texas
15	Abbott Laboratories	North Chicago, Ill.
16	USV Pharmaceutical Corp.	New York, N.Y.
17	The Upjohn Company	Kalamazoo, Mich.
18	Ayerst Laboratories	New York, N.Y.
19	Lessere-Wertheim, Inc.	Hartford, Conn.
20	The Emko Company	St. Louis, Mo.
21	Barrington Research Associates	Cranbury, New Jersey
22	Programmed Learning, Inc.	Garden City, N.Y.
23	Group Insurers, Inc.	New Haven, Conn.
24	Merck, Sharp & Dohme	West Point, Penna
25	Medi Card, Inc.	Stamford, Conn.
26-28	Connecticut Physicians' Art Association	
29	Kingsley-Quinn, Ltd.	New York, New York
30	Ciba Pharmaceutical Company	Summit, N.J.
31-34	Connecticut Physicians Art Association	
35	Bristol Laboratories	Syracuse, N.Y.
36-48	Scientific Exhibits	
49	The Coca Cola Company	Waltham, Mass.

Artists — Attention!

GENERAL INFORMATION: The Connecticut Physicians Art Association is planning the 1969 Art Exhibit in conjunction with the annual meeting of the Connecticut State Medical Society. The following information is submitted for guidance to art hobbyists.

WHERE: Hartford Hilton Hotel, Hartford, Conn.

WHEN: May 13, 14, 15, 1969

ELIGIBILITY: Physicians (members of Connecticut State Medical Society) and their families are cordially invited to join this group of art hobbyists. (In the case of children and other members of physician's family, kindly indicate relationship to sponsor.) All previous exhibitors are invited to show their works at this meeting, and new exhibitors are welcomed. Works eligible will include oil, water color, tempora, black and white etchings, photography, pastels, collages, mixed media and sculpture. Paintings over 24 x 30 will be hung only at the discretion of the art committee depending upon available space.

JUDGING: Art works will be judged in four categories; 1. children under 16 yrs. (children over 16 yrs. will be judged with adults); 2. beginners; 3. intermediaries; 4. professionals. Pictures should be framed and wired for hanging. The exhibit will be judged by professional artists.

Under no condition can art work be accepted after MAY 11th.

COST: A hanging fee of two dollars (\$2.00) will be charged for each entry and fifty cents (\$.50) for children under 16 yrs. with two entries per artist. (Space requirements have caused our limiting the entries to two this year, as just noted.)

HOW TO APPLY: Entry blanks will be mailed to former exhibitors and also may be obtained by writing to the addresses of the committee listed below. One half of the entry blank should be submitted to me at the below listed address with your check prior to April 30, 1969. The other half should be attached to the picture. Make checks payable to Connecticut Physicians Art Association. Please fill in entry blanks com-

pletely so that entry can be categorized easily in the above noted four divisions.

SUBMITTING: Art works must be submitted to a representative of the Art Association in the lobby of the Hartford Hilton Hotel on Sunday, May 11, between the hours of 12 and 3 P.M. Parking temporarily near the side entrance is possible for the few minutes involved in dropping off these art works. It may be possible to aid exhibitors with the transportation of art works by contacting members of the committee noted below. These art works must be picked up on Thursday, May 15, between 12 and 4 P.M. Members of the art committee or their representatives will be in attendance at the display throughout the exhibit at the state meeting. The Connecticut State Medical Society, the hotel, (nor the Art Association) can assume no responsibility for loss or damage of any cause to art works.

If further information is needed, the following persons may be contacted:

Stewart J. Petrie, M.D., President, 56 Minerva St., Derby, Conn.; Mrs. Orvan Hess, Vice President, 29 Old Orchard Rd., North Haven, Conn.; Mrs. John Shoukimas, Chairman, Art Committee, Woman's Auxiliary, CSMS, 26 Pheasant Hill Dr., West Hartford, Conn.; Edward Williams, M.D., 580 Hillside Ave., Naugatuck, Conn.; Herman Austrian, M.D., 935 White Plains Rd., Trumbull, Conn.; Donald Morrison, M.D., 26 Birch Rd., West Hartford, Conn.; Eugene Rightmyer, M.D., 114 Sherman Ave., New Haven, Conn.; Mrs. Mark Hayes, 163 Ridgewood Ave., North Haven, Conn.; Mrs. John D. Murphy, 8 E. Normandy Dr., West Hartford, Conn.; Mrs. Henry Sherwood, Penfield Hill Rd., Portland, Conn.; Mrs. Clifford Wilson, 19 East Town St., Norwich, Conn.

From the reports, comments and compliments received from the past years' shows, this seems to be a point of major interest of the annual meeting of the Connecticut State Medical Society. We therefore wish to thank the art hobbyists and encourage their continued participation in this exhibit.

Stewart J. Petrie, M.D., *President*
Connecticut Physicians Art Association

177th ANNUAL MEETING
of the
CONNECTICUT STATE MEDICAL SOCIETY

Hartford Hilton Hotel
10 Ford Street, Hartford, Connecticut

May 13, 14, 15, 1969

COMMITTEE ON PROGRAM OF THE SCIENTIFIC ASSEMBLY



DR. ECKHARDT

WILLIAM F. ECKHARDT, JR., *New Canaan, Chairman*

PAUL F. McALENNEY, *New Haven*

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HOWARD LEVINE, *New Britain*

MESSAGE FROM THE PRESIDENT

The Connecticut State Medical Society will hold its 177th Annual Meeting On May 13, 14, 15 at the Hartford Hilton Hotel. The Program Committee has put forth a special effort to plan a meaningful program, which should be both instructive and timely for all physicians.

The House of Delegates is again meeting on two days, so that the Reference Committees of the House may have ample time to hold hearings on matters referred to them.

This is done also with the intention of interesting the entire membership of the Society in the business of the House. We encourage you to attend any of the Reference Committee hearings that you can and give them the benefit of your opinion.

This year, we are going to hold several round table discussions on Wednesday and Thursday. This is an experiment in a new learning technique and should prove stimulating and instructive. You must pre-register for these "learning panels"; details are outlined in the program of the meeting.

I hope you are planning to stay for the Annual Dinner of the Society. This is your opportunity to meet your colleagues, their wives, and the incoming officers of the Society. Since this is the only social affair of the year, we should give it our support.

Let us each resolve to make this meeting an outstanding success. By our attendance, we can show our appreciation to all those who have worked so hard to make it a fine meeting.

I shall look for you there.

Norman H. Gardner

GENERAL INFORMATION — READ CAREFULLY

REGISTRATION

The registration desk will be located on the mezzanine floor and everyone attending the meeting is requested to register. There will be no charge for registration and all members of the Society will be given a guest luncheon ticket when and only if they register.

PARKING

There are ample parking facilities at the hotel and in the surrounding area. If you wish, you may drive up to the door of the hotel and an attendant will park your car for you.

TELEPHONE

Telephone messages will be received at Hartford 249-5611.

LUNCHEONS

Luncheons will be served in the Cities Rooms on the Mezzanine, on May 14 and May 15 and ALL MEMBERS OF THE SOCIETY REGISTERING WILL BE THE GUEST OF THE SOCIETY. PLEASE REMEMBER A LUNCHEON TICKET WILL BE GIVEN TO MEMBERS ONLY IF THEY REGISTER.

HOTEL ACCOMMODATIONS

Persons who wish to remain overnight should make reservations not later than two weeks prior to opening date of the meeting. Reservations will be held until 6:00 P.M. on the day of arrival, unless later hour is specified. Please indicate in your letter that you are attending the Connecticut State Medical Society meeting. Your letter should be directed to the Front Office Manager, Hartford Hilton Hotel, 10 Ford Street, Hartford, Connecticut.

ANNUAL DINNER

The Annual Dinner will be held at the hotel on Wednesday, May 14, 1969. The social hour will be at 6:15 P.M. and the dinner at 7:00 P.M. All persons attending the dinner will be the guests of the Society at the social hour which will begin *promptly* at 6:15 P.M. and end *promptly* at 7:00 P.M. Your reservation for dinner should be sent in as soon as possible.

PROGRAM

General scientific sessions will be held on Tuesday, Wednesday and Thursday in the Terrace Room and Section meetings will be held in the rooms listed in the program. A new feature, "Round Table Discussion" will be held on Wednesday and Thursday mornings.

EXHIBITS

All the exhibits will be located in the ballroom. Physicians should take advantage of the opportunity to review "under one roof" what is new and timely in the goods and services available. Also new this year will be scientific exhibits.

ANNUAL MEETING OF THE HOUSE OF DELEGATES

Tuesday, May 13

TERRACE ROOM — MEZZANINE

OPENING SESSION

KENNETH F. BRANDON, *Hartford, Speaker of the House, presiding*

FRANK K. ABBOT, *Waterbury, Vice-Speaker of the House*

8:00 REGISTRATION OF DELEGATES

Continental Breakfast for Delegates and Official Guests

8:30 CALL TO ORDER

11:45 REFERENCE COMMITTEE HEARINGS—Cities Rooms

12:30 LUNCHEON FOR DELEGATES AND OFFICIAL GUESTS—Fourth Floor Rooms

6:30 RECEPTION AND DINNER FOR DELEGATES AND OFFICIAL GUESTS—Cities Rooms—Mezzanine

Wednesday, May 14

TERRACE ROOM — MEZZANINE

FINAL SESSION

8:00 REGISTRATION OF DELEGATES

Continental Breakfast for Delegates and Official Guests

8:30 CALL TO ORDER

12:30 ADJOURNMENT



WALTER R. ANYAN, JR.
New Haven, Conn.



MARY S. CALDERONE
New York, New York



CHARLES C. DAHLBERG
New York, New York



J. ROSWELL GALLAGHER
New Haven, Conn.

SCIENTIFIC PROGRAM

Tuesday, May 13

- 1:00 REGISTRATION—Mezzanine
OPENING OF EXHIBITS—Ballroom—Mezzanine

TERRACE ROOM

- 1:30 CALL TO ORDER AND ADDRESS OF WELCOME
NORMAN H. GARDNER, *East Hampton, Connecticut; President of the Society*
Presiding: PAUL F. McALENNEY, *New Haven, Connecticut*

PANEL ON MEDICAL, BEHAVIORAL, ENDOCRINE PROBLEMS IN ADOLESCENTS

Moderator: WALTER R. ANYAN, JR., *New Haven, Connecticut; Instructor of Pediatrics and Medicine; Yale University School of Medicine, Associate Pediatrician, Yale-New Haven Hospital*

- 1:45 SEX AND SEXUALITY: EMERGING CONCEPTS IN THE EDUCATIONAL PROCESS
MARY S. CALDERONE, *New York City; Executive Director, Sex Information and Education Council of the U.S., (SIECUS)*
- 2:20 DRUG USE, ABUSE AND DEPENDENCY IN THE ADOLESCENT PERIOD
CHARLES CLAY DAHLBERG, *New York City; Training and Supervisory Analyst, The William A. White Institute; Visiting Psychiatrist, Bellevue Hospital*
- 2:55 DISCUSSION—QUESTIONS AND ANSWERS
Principal Discussant: J. ROSWELL GALLAGHER, *New Haven, Connecticut; Clinical Professor of Pediatrics, Yale University School of Medicine; Attending Pediatrician, Yale-New Haven Hospital*

- 3:30 INTERMISSION TO VISIT EXHIBITS

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON PEDIATRICS (Hezekiah Beardsley Club)

4:00 Room 404

President: NOAH BARYSH, *New Milford*
Secretary: ESTELLE SIKER, *Hartford*

BUSINESS MEETING—Election of Officers

Program

HEALTH PLANNING, PREVENTIVE MEDICINE AND THE PHYSICIAN

GEORGE WALKER, *Hartford, Connecticut; Director, Comprehensive Health Planning, Connecticut State Department of Health*

Tuesday May 13

CONNECTICUT DISTRICT BRANCH—AMERICAN PSYCHIATRIC ASSOCIATION

4:00 Room 440

President: ROBERT L. ARNSTEIN, *Hamden*
Secretary: ELLIS A. PERLSWIG, *New Haven*

The program will be a panel discussion, keynoted by several well known speakers, on the problems and issues in working with adolescents.

SECTION ON UROLOGY

4:00 Room 436

President: JOHN B. GOETSCH, *New Haven*
Secretary: ARNOLD M. BASKIN, *New Haven*

PHYSIOLOGIC AND CLINICAL ASPECTS OF URETERAL PROBLEMS IN CHILDHOOD

ROBERT M. WEISS, *New Haven, Connecticut; Assistant Professor of Urology, Yale University School of Medicine*

PROGRAM ON STUDENTS IN REBELLION

THE ROLE OF THE SCHOOLS IN MEETING THE CHALLENGE

8:00 P.M. TERRACE ROOM

Presiding: NORMAN H. GARDNER, *East Hampton, Connecticut*
President of the Society

Moderator: ROSWELL D. JOHNSON, *Providence, Rhode Island; Director, Health Services, Lecturer in Health Science, Brown University*

Panelists: WILLIAM C. FRENCH, Ph.D. *New Canaan, Connecticut; Superintendent, New Canaan Public Schools, Visiting Professor, Fairfield University*
(Representing the Public School Segment)

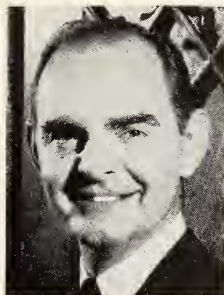
MR. JOHN C. ESTY, JR., *Watertown, Connecticut; Headmaster, Taft School; Former Associate Dean, Amherst College*
(Representing the Private School Segment)

MR. HENRY S. COLEMAN, *New Canaan, Connecticut; Dean of Freshmen, Columbia College, New York City*
(Representing the College Segment)

DISCUSSION—Questions and Answers



ROSWELL D. JOHNSON
Providence, R.I.



WILLIAM C. FRENCH
New Canaan, Conn.



JOHN C. ESTY, JR.
Watertown, Conn.



HENRY S. COLEMAN
New Canaan, Conn.

Wednesday, May 14

8:30 FINAL SESSION OF HOUSE OF DELEGATES—Terrace Room

SCIENTIFIC PROGRAM

9:00 REGISTRATION—Mezzanine

(This year the Program Committee is experimenting with a new learning technique in which members of the Society are invited and encouraged to participate. Four of these Round Table Discussions, or "Learning Panels", will be held on Wednesday, May 14th, and four others on Thursday, May 15th, in the forenoon. The subject, time and place for each is published in the Program which follows. The respective "Learning Panels" will be chaired by experienced physicians who will lead their groups, of not more than 15 participants, through in-depth examination of the topics assigned. Active participation in the group discussion will be limited to members who have pre-registered (registration form enclosed with program). It is planned to send, in advance, to those who pre-register source materials pertinent to the subject to be explored. Members who have not pre-registered will be welcome to attend the Panels as observers only, within the limits of available seating capacity.)

ROUND TABLE DISCUSSIONS

10:00-11:30 Fourth Floor in Rooms Designated

SOME PITFALLS IN INTERPRETING ELECTROCARDIOGRAMS—Room 424

Group Leader: EDGAR LICHTSTEIN, *New Britain, Connecticut*

EVALUATION OF COAGULATION DISORDERS—Room 420

Group Leader: STUART C. FINCH, *New Haven, Connecticut*

NEW CONCEPTS IN PATHOGENESIS AND TREATMENT OF DIABETIC STATE—Room 416

Group Leader: DAVID S. WILCOX, *Hartford, Connecticut*

NEW MANAGEMENT OF RH INCOMPATIBILITY—Room 412

Group Leader: JOHN T. QUEENAN, *Greenwich, Connecticut*

11:30 INTERMISSION TO VISIT EXHIBITS

12:30 LUNCHFON—Cities Rooms

TERRACE ROOM

Presiding: HOWARD LEVINE, *New Britain, Connecticut*

SYMPOSIUM ON CURRENT TECHNIQUES IN THE MANAGEMENT OF MYOCARDIAL INFARCTION

1:30 CORONARY CARE EXPERIENCES AND FUTURE DIRECTIONS

JAMES K. COOPER, *Arlington, Virginia*; Chief, Control Section, Heart Disease and Stroke Control Program, U.S. Public Health Service; Clinical Instructor in Medicine, George Washington University Medical School

2:00 NEW AND OLD DRUGS IN THE TREATMENT OF MYOCARDIAL INFARCTION AND ITS COMPLICATIONS

EDMUND H. SONNENBLICK, *Boston Massachusetts*; Assistant Professor, Harvard Medical School; Co-Director, Cardiovascular Unit, Peter Bent Brigham Hospital

2:30 NEW ELECTRONIC AIDS IN THE MANAGEMENT OF MYOCARDIAL-INFARCTION AND ITS COMPLICATIONS

LESLIE A. KUHN, *New York City*; Associate Professor of Medicine, Mt. Sinai School of Medicine; Associate Attending Cardiologist, Mt. Sinai Hospital

3:00 DISCUSSION—Questions and Answers

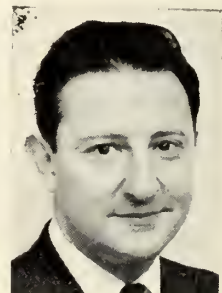
3:30 INTERMISSION TO VISIT EXHIBITS



JAMES K. COOPER
Arlington, Virginia



EDMUND H. SONNENBLICK
Boston, Mass.



LESLIE A. KUHN
New York, New York

Wednesday, May 14

MEETINGS OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON DERMATOLOGY

3:30 Room 424

President: HASKELL M. ROSENBAUM, *Waterbury*
Secretary: NEVILLE KIRSCH, *Hartford*

DIAGNOSIS AND TREATMENT OF COMMON HYPERKERATOTIC LESIONS OF THE FOOT
ROYAL M. MONTGOMERY, *New York City; Director, Dermatology Service, Roosevelt Hospital and St. John's Queens Hospital*

PROPER BALANCING OF THE FOOT

MR. WILLIAM V. LOCASCIO, *New York City; Orthotist*

SECTION ON INTERNAL MEDICINE

4:00 Room 420

President: HARVEY N. MANDELL, *Norwich*
Secretary: VINCENT A. DELUCA, JR., *Derby*

AZOTEMIA—DRUG INDUCED?

MICHAEL Z. LAZOR, *Hartford, Connecticut; Attending Staff, Hartford Hospital*

JOINT MEETING

SECTION ON OBSTETRICS AND GYNECOLOGY

President: EDWIN J. T. MOORE, *Waterbury*
Secretary: PETER A. GOODHUE, *Stamford*

SECTION ON PATHOLOGY

President: ROGER K. GILBERT, *Waterbury*
Secretary: SEBASTIAN J. GALLO, *Middletown*

4:00 Rooms 408-412

THE CONSERVATIVE TREATMENT OF OVARIAN CANCERS IN YOUNG WOMEN

ROBERT E. SCULLY, *Boston, Massachusetts; Associate Clinical Professor of Pathology, Harvard Medical School; Pathologist, Massachusetts General Hospital*

SECTION ON OPHTHALMOLOGY

4:00 Boston-Buffalo Rooms

President: ANDREW S. WONG, *New Haven*
Secretary: DANIEL M. TAYLOR, *New Britain*

4:00 BUSINESS MEETING

5:00 PRACTICAL PLASTIC SURGERY

ARTHUR G. DEVOE, *New York City; Professor and Chairman, Department of Ophthalmology, Columbia Presbyterian Medical Center*

6:15 SOCIAL HOUR

7:00 THE SECTION DINNER will be held in conjunction with the annual dinner of the Society in the Terrace Room. Return reservations to CSMS office.

SECTION ON PHYSICAL MEDICINE

4:00 Rooms 436-440

President: OTTO G. GOLDKAMP, *Hartford*
Secretary: EDWIN L. LYTLE, *Wallingford*

PHYSICAL ENERGY REQUIREMENTS OF ACTIVITIES AFTER MYOCARDIAL INFARCTION AND STROKE

EDWARD E. GORDON, *Chicago, Illinois; Director, Department of Physical Medicine and Rehabilitation, Michael Reese Hospital and Medical Center*

Wednesday, May 14

SECTION ON PREVENTIVE MEDICINE

4:00 New York Room

Chairman and Secretary: J. HOWARD JOHNSTON, *West Hartford*

CARDIO-ALERT SYSTEM—ECG MONITORING AND TRANSMISSION FROM AMBULANCES

ROBERT J. HUSZAR, *Hartford, Connecticut; Director of Research, Cardiovascular-Pulmonary Section, St. Francis Hospital*

SECTION ON PROCTOLOGY

4:00 Washington Room

President: BERNARD J. KAPLAN, *Hartford*
Secretary: SANFORD SAVIN, *Bridgeport*

CONSERVATIVE SURGICAL MANAGEMENT OF RECTAL CANCER

MALCOLM C. VEIDENHEIMER, *Boston, Massachusetts; Colon and Rectal Surgeon, Lahey Clinic*

CONNECTICUT DIABETES ASSOCIATION

4:00 Room 416

President: WILLEM F. VAN ECK, *East Haven*
Secretary: JAMES C. HART, *Hartford*

THE NEUROLOGICAL COMPLICATIONS OF DIABETES MELLITUS

LEWIS L. LEVY, *New Haven, Connecticut*

COMPAC—CONNECTICUT MEDICAL
POLITICAL ACTION COMMITTEE

Room 404

2:00 BUSINESS MEETING

Wednesday, May 14

ANNUAL DINNER OF THE SOCIETY

HARTFORD-HILTON HOTEL

10 Ford Street, Hartford

Social Hour 6:15 P.M.

Dinner 7:00 P.M.

Program

OPENING REMARKS

NORMAN H. GARDNER, *East Hampton*

Presiding: STEVENS J. MARTIN, *Hartford; President*

PRESENTATION OF GUESTS AND DELEGATES FROM STATE MEDICAL SOCIETIES

FIFTY YEAR MEMBERSHIP AWARD

Stanton Reinhart Smith, *Bridgeport*

Claudius Virgil Calvin, *Fairfield*

William James Fay, *Hartford*

Samuel Maislen, *Hartford*

Edwin Godwin Reade, *Watertown*

Mark Thomas Sheehan, *Wallingford*

MUSICAL PROGRAM

Wednesday, May 14

WOMAN'S AUXILIARY TO THE CONNECTICUT STATE MEDICAL SOCIETY
TWENTY-FIFTH ANNUAL MEETING

WADSWORTH ATHENEUM
25 Atheneum Square, Hartford Connecticut

President: MRS. CLARENCE W. HARWOOD, *Middletown*

Recording Secretary: MRS. MELVILLE Y. ALDERMAN, *West Hartford*

Corresponding Secretary: MRS. DONALD E. MILLER, *Middletown*

- 1:00 LUNCHEON
2:00 BUSINESS MEETING
3:00 TOUR OF THE ATHENEUM

Thursday, May 15

- 8:30 REGISTRATION—Mezzanine

ROUND TABLE DISCUSSIONS

9:00-10:30 Fourth Floor in Rooms Designated

FACIAL PAIN—Room 424

Group Leader: LEWIS L. LEVY, *New Haven, Connecticut*

MANAGEMENT OF BREAST CANCER METASTASES—Room 420

Group Leader: IRA S. GOLDENBERG, *New Haven, Connecticut*

EVALUATION AND TREATMENT OF HEARING DISORDERS—Room 416

WHAT TEST AND TREATMENTS, WHEN AND WHY?

Group Leaders: ROBERT S. ROSNAGLE, *New Haven, Connecticut*

DAVID S. GREEN, Ph.D., *New Haven, Connecticut*

TRAUMA TO THE HAND—Room 412

Group Leaders: KRISTAPS J. KEGGI, *New Haven, Connecticut*

JAMES A. ALBRIGHT, *New Haven, Connecticut*

- 10:30 INTERMISSION TO VISIT EXHIBITS

TERRACE ROOM

Presiding: WILLIAM F. ECKHARDT, JR., *New Canaan, Connecticut*

PANEL ON ORGAN VISUALIZATION BY TWO COMPLEMENTARY METHODS

A. Radioisotope Scanning 11:00-12:30

B. Arteriography 1:30-3:00

- 11:00 NEWER DYNAMIC TECHNIQUES

MERRILL A. BENDER, *Buffalo, New York*; Chief, Department of Nuclear Medicine, Roswell Park Memorial Institute; Chairman, American Board of Nuclear Medicine

- 11:30 CURRENT STATUS OF NUCLEAR MEDICINE

HENRY N. WAGNER, JR., *Baltimore, Maryland*; Professor of Radiology and Radiological Science, Associate Professor of Medicine, The Johns Hopkins Medical Institutions

- 12:00 DISCUSSION—Questions and Answers

- 12:30 LUNCHEON—Cities Rooms

INTERMISSION TO VISIT EXHIBITS



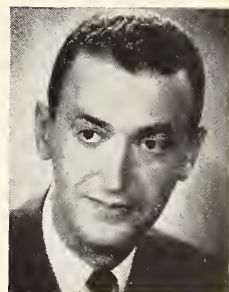
MERRILL A. BENDER
Buffalo, New York



HENRY N. WAGNER, JR.
Baltimore, Maryland



DOUGLASS F. ADAMS
Boston, Mass.



STANLEY BAUM
Philadelphia, Penn.

Thursday, May 15

PANEL ON ARTERIOGRAPHY

Moderator: JACK L. WESTCOTT, *Hartford*

- 1:30 WHY AN ANGIOGRAM?
DOUGLASS F. ADAMS, *Boston Massachusetts; Instructor in Radiology, Harvard Medical School; Associate in Radiology, Peter Bent Brigham Hospital*
- 2:00 RECENT ADVANCES IN ABDOMINAL ARTERIOGRAPHY
STANLEY BAUM, *Philadelphia, Pennsylvania; Associate Professor of Radiology, University of Pennsylvania School of Medicine; Associate Radiologist, Graduate Hospital*
- 2:30 DISCUSSION—Questions and Answers
- 3:00 INTERMISSION TO VISIT EXHIBITS

PROGRAM ARRANGED WITH THE CONNECTICUT SOCIETY OF
AMERICAN BOARD SURGEONS

Presiding: WILLIAM T. LIVINGSTON, *New Britain*

- 3:30-5:00 BASIC PRINCIPLES IN THE EMERGENCY CARE OF INJURIES OF THE HAND AND FACE
ROBERT A. CHASE, *Palo Alto, California; Professor and Executive, Department of Surgery, Stanford University School of Medicine*

MEETING OF SECTIONS OF THE SOCIETY AND GUEST ORGANIZATIONS

SECTION ON ALLERGY

4:00 Room 408

President: A. ARTHUR FIERBERG, *Hartford*

Secretary: EDWARD J. CONWAY, *Hartford*

THE USE AND ABUSE OF STEROID HORMONE

BRUCE F. BOWER, *Hartford, Connecticut; Clinical Endocrinologist, Hartford Hospital*

SECTION ON ANESTHESIA

Boston-Buffalo Rooms

President: RICHARD F. GRANT, *Cromwell*

Secretary: HENRY T. BONNEY, *Hartford*

3:00 EXECUTIVE MEETING

4:00 BUSINESS MEETING

5:00 GUEST SPEAKER

RICHARD GILBERT, *Professor of Anesthesia, McGill University, Montreal, Canada* (Subject to be Announced)

6:00 SOCIAL HOUR—New York Room

7:00 DINNER—Rooms 408-412

SECTION ON GENERAL PRACTICE

4:00 Room 424

President: D. WILLIAM PASQUARIELLO, *Bridgeport*

Secretary: LEO P. GIARDI, *Hartford*

The program will be a discussion on the certification examination for the American Board of Family Practice. Speakers will be announced.

SECTION ON ORTHOPEDICS

4:00

HUNT MEMORIAL BUILDING

230 Scarborough Street, Hartford

President: NED M. SHUTKIN, *New Haven*

Secretary: CHARLES T. FLYNN, JR., *Meriden*

ATHLETIC INJURIES OF LOWER EXTREMITIES

JOSEPH D. GODFREY, *Buffalo, New York; Clinical Professor of Orthopedics, State University of New York*

Thursday, May 15

JOINT MEETING

SECTION ON NEUROLOGY

President: GILBERT H. GLASER, *New Haven*

Secretary: JOHN C. MOENCH, *New Haven*

SECTION ON NEUROSURGERY

President: WILLIAM T. GERMAN, *New Haven*

Secretary: ROBERT H. STURMAN, *Waterbury*

4:00 New York-Washington Rooms

Round table discussion of, "Angiographic and Nuclear Medicine Techniques as Applied to the Nervous System".

SECTION ON OTOLARYNGOLOGY

4:00 Room 412

President: MILTON L. JENNES, *Waterbury*

Secretary: ROBERT S. ROSNAGLE, *New Haven*

THE PROBLEMS OF ASSISTED RESPIRATION

DOUGLAS P. BRYCE, *Toronto, Ontario, Canada; Otolaryngologist-in-Chief, Toronto General Hospital*

SECTION ON RADIOLOGY

Room 420

President: KENNETH R. KAESS, *Waterbury*

Secretary: ROBERT F. KILEY, *Hartford*

1:30 Members of the Section on Radiology will attend the Panel on Arteriography which will be held in the Terrace Room.

3:00 BUSINESS MEETING—Room 420

3:30 Section members are invited to attend the program arranged by the Connecticut Society of American Board Surgeons in the Terrace Room.

ASSOCIATION OF MEDICAL EXAMINERS FOR CONNECTICUT

12:30 Rooms 436-440

President: SAMUEL B. RENTSCH, *Derby*

Secretary: MARCUS E. COX, *Waterbury*

12:30 LUNCHEON FOR MEDICAL EXAMINERS, CORONERS, AND GUESTS (Dutch Treat)

Guest Speaker: Senator JAY W. JACKSON, *Hartford*

1:45 BUSINESS MEETING—Election of Officers

2:00 Members are invited to attend the scientific program in the Terrace Room

CONNECTICUT SOCIETY OF AMERICAN BOARD SURGEONS

President: WILLIAM T. LIVINGSTON, *New Britain*

Secretary: ROBERT J. WILLIAMSON, *Bristol*

3:30-5:00 TERRACE ROOM—(See General Program—Thursday 3:30 P.M.)

5:00 SOCIAL HOUR

6:00 DINNER—Terrace Room

Guest Speaker: ROBERT A. CHASE, *Palo Alto, California; Professor and Executive, Department of Surgery, Stanford University School of Medicine*

The Control of Idioventricular Rhythm in Acute Myocardial Infarction by Transvenous Intracardiac Pacing

Report of a Case

Sidney M. Richman, M.D.

The advent of coronary care units and continuous cardiac monitoring has enabled physicians to recognize and treat arrhythmias which might have previously been missed.¹ The use of a transvenous intracardiac pacemaker is now generally accepted as primary treatment for complete heart block in acute myocardial infarctions.^{2, 3} Electronic pacing in second degree heart block and sinus bradycardia is less well accepted, although some centers routinely employ a pacemaker for these complications also. However, there are only scattered reports indicating the use of a transvenous pacemaker to control arrhythmias.^{4, 5}

The following case illustrates the effective control of an idioventricular rhythm by transvenous pacing in a patient with an acute myocardial infarction. The case also shows that the usual drug modalities of treatment were either ineffective or contraindicated.

Case Report

A 52-year old white male was admitted to Mt. Sinai Hospital at 1:00 A.M. with crushing substernal chest pain. An electrocardiogram revealed an acute anteroseptal myocardial infarction. This was subsequently confirmed by a peak serum glutamic oxalacetic transaminase value of 148 and a lactic dehydrogenase of 1180. There was no antecedent history of coronary disease, hypertension or diabetes.

The patient was transferred to the coronary care unit which employs a Corbin-Farnsworth remote and central cardiac monitoring system. The patient's blood pressure remained stable at 120/80, the pulse at 80, and there were no signs of congestive heart failure. For the initial 8 hours his hospital course was uneventful. However, the cardiac nurses then noted the onset of a sinus bradycardia of 55 and the occurrence of ventricular ectopic beats (tracing A) at approximately 10-15 per minute. There was no increase

in cardiac rate after the intravenous administration of atropine grains 1/75th. Intravenous therapy was then initiated with lidocaine (2 grms. per 500 cc 5% dextrose and water). Shortly after the start of the drug, the patient began to develop runs of idioventricular rhythm with the same configuration as the ectopic beats (tracing B & C). The ventricular rate was 68 and for several minutes there was competition between the sinus and ventricular pacemaker as tracings B and C illustrate. The lidocaine was discontinued, but the idioventricular rhythm became sustained with only sporadic sinus beats coming through (tracing D). Throughout this arrhythmia the patient was in no discomfort and his blood pressure remained stable. As will be discussed later, several drugs were considered as treatment, but it was decided to insert a transvenous pacemaker. An Electroath bipolar pacemaker was inserted through the right brachial vein and passed into the right ventricle. Pacing was accomplished by a Medtronic battery powered pacemaker #5800 at 6.3 M.A. and 90 beats per minute (tracing E). This completely abolished the ventricular rhythm. It was noted that when the pacemaker rate was experimentally dropped below 90, there was competition between the ventricular and electronic pacemakers. This substantiated that a more rapid rate could suppress the ventricular pacemaker.

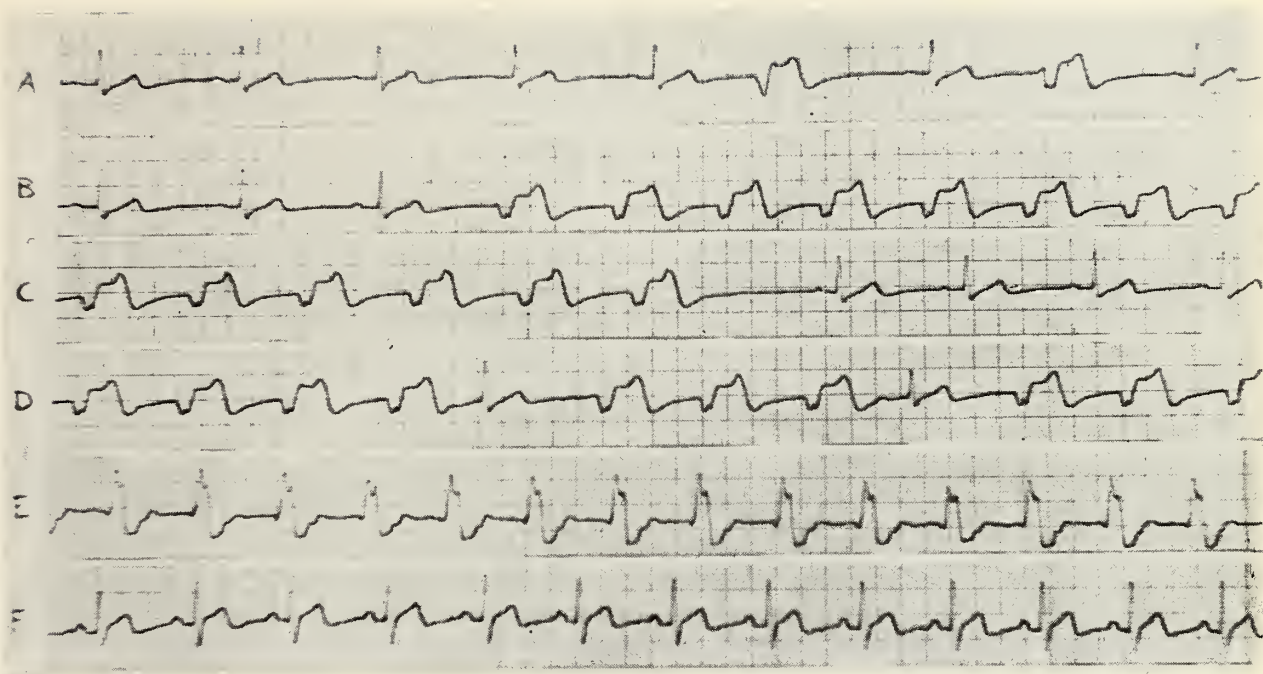
Approximately four hours after insertion of the pacemaker, the cardiac nurses again noted the occurrence of the idioventricular rhythm. It was determined that the pacemaker had slipped out of position, and this was repositioned without difficulty—again with abolition of the ventricular rhythm. The pacemaker was left in position for 48 hours. During this time, attempts to turn it off resulted in a recurrence of the idioventricular rhythm. After 48 hours, it was found that that patient now had a sinus rhythm of 80 with no further evidence of ectopic activity (tracing F). The catheter was left in position for an additional 24 hours with the power off, and was subsequently removed. The patient continued to have a sinus rhythm of 80 and his subsequent hospital course was uneventful.

Discussion

The decision to employ electronic pacing to treat this patient was dictated by a virtual exclusion of most of the drugs currently available for ventricular arrhythmias. It was noted that the

DR. SIDNEY M. RICHMAN, Director, Section of Cardiology, Mount Sinai Hospital, Hartford.

The cardiac monitoring equipment used in the coronary care unit was provided through a grant by the Hartford Heart Association.



The above electrocardiograms were taken by remote control from a central cardiac monitor and represent standard lead I.

A—sinus bradycardia with evidence of ventricular beats.

B & C—runs of idioventricular rhythm of the same configuration as the initial ventricular ectopic beats showing the mode of onset and the mode of termination.

D—sustained idioventricular rhythm with only occasional evidence of sinus activity.

E—the rhythm is now driven by the intracardiac pacemaker with no evidence of ectopic activity.

F—following the removal of the pacemaker, the patient remained in sinus rhythm at 80 per minute and no abnormal ventricular activity.

idioventricular rhythm became sustained after the lidocaine drip was initiated. Although such paradoxical responses have been seen with quinidine,⁵ they have not been reported with lidocaine, and the sequence of events in this patient may have been coincidental. However, we were naturally reluctant to push lidocaine under these circumstances. Quinidine and procaine amide were also ruled out as they have a similar mechanism of action to lidocaine in addition to their hypotensive properties.⁶ Although atropine is not completely innocuous,⁷ its safety margin is such that it is usually given as the initial treatment of symptomatic sinus bradycardia. It was anticipated that the ectopic ventricular activity in this patient would be eliminated if the sinus pacemaker had a more rapid rate. However, atropine failed to produce any increase in cardiac rate. Diphenyl hydantoin appears to be effective in ventricular arrhythmias due mainly to digitalis intoxication and is contraindicated in sinus bradycardia.⁸ Propranolol, while effective in ventricular arrhythmias, also enhances bradycardia due to unopposed vagal action,⁹ so that this drug is also contraindicated. Both

isoproterenol and epinephrine can speed up a sinus bradycardia, but are potent enhancers of ectopic ventricular activity¹⁰ and, in this patient, would have easily precipitated ventricular tachycardia or fibrillation. The use of a cardiac pacemaker was therefore the most physiologic and rational approach.

Recently, Rothfeld et al¹¹ have questioned whether an idioventricular rhythm in acute myocardial infarction should be treated at all. They described this rhythm in 36 of 100 consecutive patients with acute myocardial infarction. The rhythm and circumstances were very similar to the patient in this case report—i.e. occurring in the presence of a sinus bradycardia. In none of their patients did the idioventricular rhythm progress to ventricular fibrillation and the rhythm did not affect the prognosis adversely. They felt that the idioventricular rhythm may actually be a protective mechanism to prevent sustained bradycardia. However, in all of their patients, this rhythm was transient—lasting 4 to 30 beats. It was noted that the idioventricular rhythm in our patient was sustained for close to 48 hours, and would recur when-

ever the pacemaker was turned off. Although our patient did not appear to be adversely effected by the rhythm, and there was no evidence of hypotension or congestive heart failure, one would be reluctant to let this rhythm remain untreated. Any ventricular rhythm in acute myocardial infarction is so unpredictable, that it is liable to progress to ventricular tachycardia, ventricular fibrillation, or cardiac arrest at any time.¹ With a functioning pacemaker in place, the physician has much better and definitive control of the patient.

The use of a transvenous pacemaker to control ventricular arrhythmias is not new.^{4, 5} It has been used to control ventricular tachycardia and ventricular fibrillation induced by permanently implanted pacemakers.^{12, 13} However, it is suggested in this report, that the pacemaker may be used more effectively and with more certainty than the various antiarrhythmic drugs in the control of a ventricular rhythm, especially when the rhythm arises in the presence of a sinus bradycardia.

Summary

A case is presented of an idioventricular rhythm occurring in the presence of sinus bradycardia in a patient with an acute myocardial infarction. The rhythm was successfully treated by a transvenous cardiac pacemaker in a situation where the currently available antiarrhythmic drugs were contraindicated or ineffective.

Bibliography

1. Meltzer, L. E. and Kitchell, J. B. The Incidence of Arrhythmias Associated with Acute Myocardial Infarctions. *Progress in Cardiovasc. Dis.* 9:50-63, 1966.

2. Paulk, E. A. and Hurst, J. W. Complete Heart Block in Acute Myocardial Infarction. A Clinical Evaluation of the Intracardiac Bipolar Catheter Pacemaker. *Am. J. Cardiol.* 17:695-706, 1966.
3. Sowton, E. The Use of Artificial Pacemaking in Cardiac Resuscitation. *Proc. Royal Soc. of Med.* 57:368-372, 1964.
4. Sowton, E., Leatham, A., and Carson, P. The Suppression of Arrhythmias by Artificial Pacemaking. *Lancet* 2:1098-1100, 1964.
5. Herman, D. F. and Helwig, J. Jr. Suppression of Ventricular Arrhythmias by Transvenous Intracardiac Pacing. *J.A.M.A.* 195:1150-1153, 1966.
6. Harrison, D. C., Sprouse, J. H., and Morrow, A. G. The Antiarrhythmic Properties of Lidocaine and Procaine Amide. *Circula.* 28:486-491, 1963.
7. Averill, K. H. and Lamb, L. E. Less Commonly Recognized Actions of Atropine on Cardiac Rhythm. *Am. J. Med. Sci.* 237:304-318, 1959.
8. Rosen, M., Lisak, R., and Rubin, I. L. Diphenylhydantoin in Cardiac Arrhythmias. *Am. J. Cardiol.* 20:674-678 1967.
9. Stepan, S. A. Unwanted Effects of Propranolol. *Am. J. Cardiol.* 18:463-468, 1966.
10. Zoll, P. M., Linenthal, A. J., Gibson, W., Paul, M. H., and Norman, L. R. Intravenous Drug Therapy of Stokes-Adams Disease. *Circula.* 17: 325-338, 1958.
11. Rothfeld, E. L., Zucker, I. R., Parsonnet, V., and Alinsonorm, C. A. Idioventricular Rhythm in Acute Myocardial Infarction. *Circula.* 37:203-209, 1968.
12. McCallister, B. D., McGoon, D. C., and Connolly, D. C. Paroxysmal Ventricular Tachycardia and Fibrillation without Complete Heart Block. Report of a Case Treated with a Permanent Internal Cardiac Pacemaker. *Am. J. Cardiol.* 18:898-903, 1966.
13. Thind, G. S., Nusbaum, M., Blakemore, W. S., and Bellet, S. Ventricular Arrhythmias in a Patient with Artificial Pacemakers. *Am. J. Cardiol.* 20:730-734, 1967.

Management of Rh-sensitized Pregnancies

Leonard A. DeFusco, M.D., James F. Loftus, M.D.
and Charles Zmijeski, Jr., M.D.

In 1961 Liley demonstrated a good correlation between the height of the 450 m μ peak and fetal outcome in Rh-sensitized pregnancies. He also suggested a practical method of management for such pregnancies.³ Later, Liley performed the first successful intrauterine intraperitoneal fetal transfusion.⁴

This paper reports our initial experiences with these techniques as utilized in a community hospital.

Ninety-three amniocenteses were performed on 44 isoimmunized patients, of which 35 were private and 9 were ward cases. Under local anesthesia a 20-gauge spinal needle was usually introduced a few centimeters below the umbilicus and to one side of the midline in the direction of the fetal small parts. Originally the amniotic fluid was analyzed with a Beckman DU spectrophotometer, and the spectral curve was then plotted on semi-logarithmic paper. We are now using a Coleman recording spectrophotometer,* in which the specimen is continuously scanned from 340 to 700 m μ , the 450 m μ peak being calculated directly from the scan.

With the possible exception of J. J. (see text below), no maternal or fetal complications could be attributed to amniocentesis.

Nine infants proved to be Rh negative, or Rh positive but unaffected. In figure I, the 450 m μ peaks of the nine unaffected babies have been plotted on Liley's graph. Serial amniocenteses are connected by lines. Note the decidedly downward trend of all those having serial taps. All of the values, with the exception of one at 26 weeks, lie in Zone I or the lower half of Zone II. None of these babies were delivered prior to 37 weeks.

Twenty-five babies showed varying degrees of erythroblastosis, ranging from laboratory evidence only to neonatal death due to hydrops. For the

figures 2 and 3 (Liley's graph). None of these infants were considered candidates for intrauterine transfusion. Of the 20 surviving the neonatal period, 14 were managed by elective induction at 36

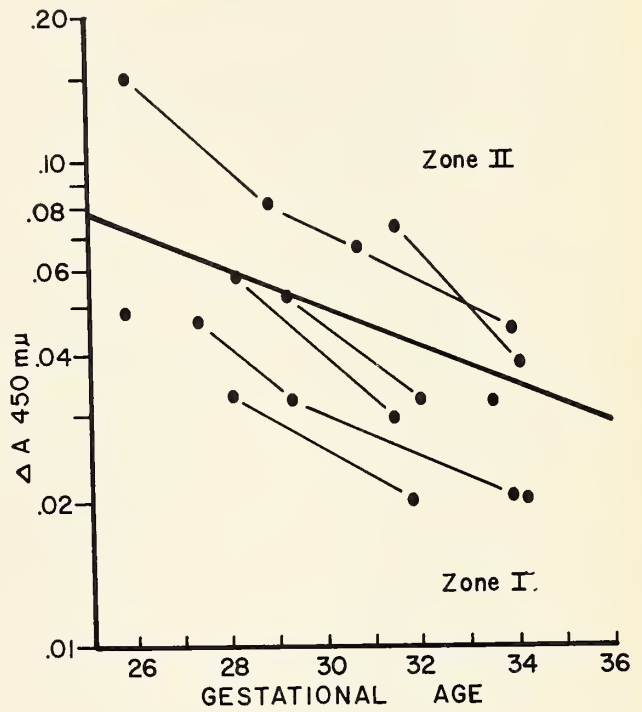


FIGURE I

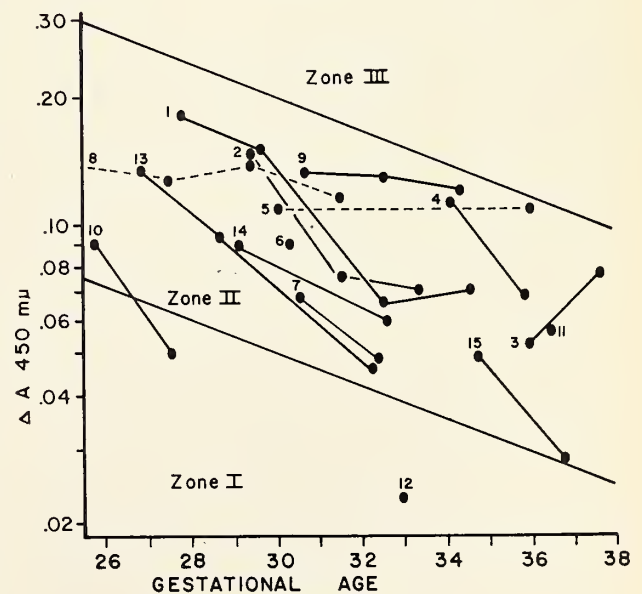


FIGURE II

* Hitachi, EPS-3T

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DR. CHARLES ZMIJESKI, JR., Assistant Attending Obstetrician and Gynecologist, St. Francis Hospital, Hartford. sake of clarity, their 450 m μ peaks are plotted in

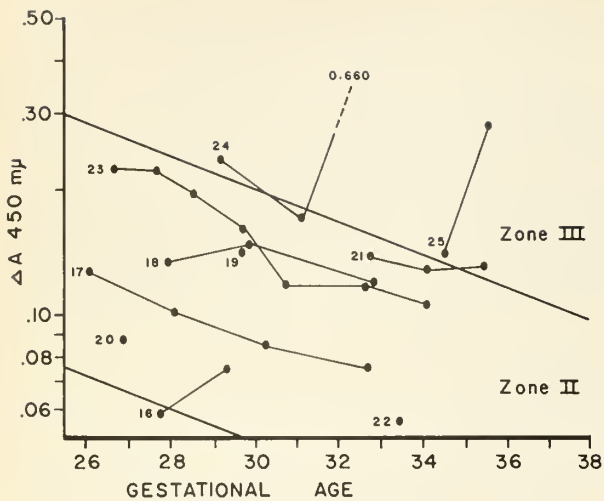


FIGURE III

weeks or beyond, and one went into spontaneous labor at 41 weeks. The 450 m μ peaks of these 15 cases are depicted in figure 2. Three infants, cases 5, 6 and 8, received four exchanges each, after having been induced at 36 weeks. Note the rather stable peaks in cases 5 (cord hemoglobin 13.5 g%; bilirubin, 5.0 mg%) and 8 (cord hemoglobin 13 g%; bilirubin, 4.9 mg%). In case 6, the cord hemoglobin was 11.5 g% and the bilirubin 5.8 mg%. In case 1, a generally downward trend was noted, but the last tap showed a slightly increased optical density over the previous tap. The infant, with cord hemoglobin of 11.5 g% and bilirubin of 6.0 mg%, received three exchanges. All the other cases in figure 2 received two or less exchanges each.

The 450 m μ peaks of the remaining ten affected newborns (cases 16 through 25) are illustrated in figure 3. Cases 16 and 17 were induced at 35 weeks. Case 16 showed a sharp increase in the 450 m μ peak at the second tap. The infant had a cord hemoglobin of 5.6 g% and a bilirubin of 8.0 mg%, and required four exchanges. Case 17 also received four exchanges but the 450 m μ peaks were gradually shrinking and the infant's cord hemoglobin was 13.3 g% and the bilirubin 5.9 mg%. Perhaps it would have been wiser to defer induction in this case.

Premature labor ensued in cases 18, 19 and 20 at 34, 31, and 36.5 weeks respectively. Case 18 was associated with abruptio placentae; the infant required three exchange transfusions. Case 20 experienced premature rupture of the membranes; no exchanges were done. There was no discernable cause for premature labor in case 19. This infant, delivered by repeat cesarean section, had a cord

hemoglobin of 8.6 g% and a bilirubin of 7.0 mg% and was exchanged twice.

There were five neonatal deaths: cases 21, 22, 23, 24 and 25. In three of the five cases (21, 24, 25) the initial 450 m μ peaks did not indicate a clear course of action. In each case the desire to attain a greater fetal maturity resulted, unfortunately, in fetal compromise. Case 21 was induced at 37 weeks and delivered of a severely affected infant (cord hemoglobin 6.5 g%; bilirubin 8.2 mg%) who suffered a cardiac arrest during an exchange. Case 24 was induced at 33.5 weeks. This infant was hydropic and expired after the second exchange. Case 25, induced at 36 weeks, was also delivered of an hydropic infant which died within minutes. Case 22 had a single tap at 33.5 weeks which revealed a 450 m μ peak of 0.057. Spontaneous delivery at 41.5 weeks resulted in a moderately severely affected infant (cord hemoglobin 9 g%; bilirubin 7.5 mg%) who received five exchange transfusions. Death at age 11 days was believed to be due to congestive heart failure secondary to congenital heart disease. Case 23 is of particular interest in that the previous pregnancy resulted in a surviving infant after three intrauterine transfusions, abdominal delivery at 34 weeks and three exchange transfusions. This is patient H. D. in table I. Seven amniocenteses were performed in this, the subsequent, pregnancy. The 450 m μ peak was calculated directed from the scan on linear paper. The initial value of 0.226 became 0.270 when the spectral curve was plotted on semilogarithmic paper. Intrauterine transfusion, however, was withheld when subsequent spectral analyses revealed shrinking 450 m μ peaks. The infant, delivered by cesarean section at 34.5 weeks, was moderately affected (cord hemoglobin 11.7 g%; bilirubin 4.9 mg%) and expired because of pulmonary atelectasis. The gradually diminishing peaks indicate that this infant should have been allowed to remain in utero longer.

Ten patients were considered candidates for intrauterine transfusion. Table I details the significant clinical data and outcome in each case. The 450 m μ peak was not calculated for patient H. D., who was the first in our series. Instead, the bilirubin was estimated quantitatively by comparing the patient's amniotic fluid spectral curve with that of a bilirubin standard. In this case the result was presumed to indicate severe fetal disease.⁹

At present, a patient is considered for intrauterine transfusion when spectral analysis reveals a bilirubin peak falling in Liley's Zone III prior to the 32nd week of gestation. In the belief that early

TABLE I

CLINICAL DATA ON PATIENTS CONSIDERED FOR INTRAUTERINE TRANSFUSION.

Patient	History	$\Delta A450 m\mu$	IUT	Outcome
J.Q.	one neonatal death	0.502 (26 wks.)	none	intrauterine death at 27 wks.
J.J.	two still-births	1.490 (27 wks.)	none	intrauterine death at 28 wks. maternal thrombocytopenia
M.G.	one neonatal death	0.910 (29 wks.)	one, 29 wks. attempt failed 30 wks.	intrauterine death 1 day after failed IUT
J.M.	one affected, survived	0.304 (28.5 wks.)	one, 29 wks. fetal ascites	spontaneous labor, 30 wks. cord bilirubin 6.0 mg%; hgb 8.5 g%. one exchange. death due to pulmonary atelectasis at 26 hours.
A.L. I	one still-birth	0.290 (27.5 wks.)	three @ 28.5, 30.5 & 33.5 wks.	induced, 35.5 wks. cord bilirubin 5.6 mg%; hgb 14.5 g%. one exchange, one booster transfusion. alive & well.
A.L. II	one still-birth. one survived after 3 IUT's	0.400 (26.5 wks.)	two @ 26.5, 28.5 wks.	premature labor with abrupt placenta, 29 wks, appeared hydropic, expired at one hour of age.
G.M.	one affected, survived	0.383 (27.5 wks.)	three @ 28, 29.5 & 32 wks. fetal ascites at last IUT.	induced, 33.5 wks. cord bilirubin 6.0 mg%; hgb 3.3 g%. 4 exchanges. alive & well.
C.L.	one affected, survived	0.300 (30.5 wks.)	one, 32 wks. hydropic.	intrauterine death at 33+ wks.
S.M.	one neonatal death. one stillbirth	0.188 (28.5 wks.)	three @ 29.5, 31.5 & 33.5 wks.	induced, 35.5 wks. cord bilirubin 4.0 mg%; hgb 16.5 g%. no exchanges. one booster transfusion. alive & well.
H.D.*	two neonatal deaths.	bilirubin 0.4 mg% (26 wks.)	three @ 27, 29, & 32 wks.	C/S, 34 wks., cord bilirubin 6.2 mg%; hgb 16 g%. 3 exchanges. alive & well.

* See text

induction is the lesser of two evils,² we no longer do intrauterine transfusions after the 32nd week. Patient S. M., was a peak of 0.188, was the second one in our series; and, according to our current criteria, would not now be considered for fetal transfusion unless subsequent amniotic fluid analysis revealed a Zone III 450 $m\mu$ peak.

In two cases, J. Q. and J. J., intrauterine death supervened before fetal transfusion could be performed. Patient J. J. is of special interest. Five days after a very difficult amniocentesis (8 attempts), the patient was admitted for intrauterine transfusion. However, no fetal heart could be heard. The patient had complained of severe, intermittent epigastric and right upper quadrant pain during the three days preceding admission. She appeared pale and there was a suggestion of scleral icterus. The blood pressure was 160/110 and there was 3+

edema of the feet and ankles. Abdominal examination initially revealed much spasm and tenderness in the right upper quadrant, so that a surgical abdomen was seriously considered. Subsequently, laboratory studies revealed a mild hemolytic process and a markedly prolonged bleeding time. The platelet count was 38,000 per cu. mm. At about the sixth hospital day the patient began to show much symptomatic improvement—without specific therapy. Nine days after admission, spontaneous labor resulted in the delivery of a premature still-born male. There was no evidence of placental abruption or fetal trauma. All abnormal studies quickly returned to normal and she has done well. No relationship to the amniocentesis could be established.

Eight fetuses received 17 intrauterine transfusions, resulting in two intrauterine deaths, two

neonatal deaths, and four surviving infants. Two fetuses were found to be hydropic at the time of the initial intrauterine transfusion. Neither survived. Because of the dismal results known to attend intrauterine transfusion of hydropic fetuses,⁵ attempts to salvage such infants should probably be restricted to premium babies. Patient M. G., although not obviously hydropic, had a very high bilirubin peak, 0.910. Bishop et al feel that fetal transfusion is contraindicated when the 450 m μ peak exceeds 0.600.⁶ Occasionally, however, fetuses with higher bilirubin peaks have been salvaged.⁶

All intrauterine transfusions are performed in our radiology department. With the aid of an image intensified system,* to which a closed circuit television unit is attached, a 16 gauge Touhy needle is directed into the fetal abdomen. Type O-negative blood, cross-matched with the mother and packed to a hemoglobin concentration of approximately 20 g%, is then infused directly through the Touhy needle. The volume administered has varied from 80 to 150 cc. depending upon the fetal age and the resistance imparted to the infusing syringe. Prophylactic antibiotics have not been used.

Errors in needle placement have resulted in penetration of fetal bowel, bladder, retroperitoneal space, pleural space and pericardial sac—all without apparent adverse fetal effect.

Summary

When the 450 m μ peak is calculated from an absorption curve on linear paper (case 23), the value obtained is somewhat lower than when this determination is made from a curve plotted on semilogarithmic paper. Generally, the difference will not be of such magnitude as to effect a change in management. However, particularly when a borderline value is obtained from the linear scan, the curve must be replotted on semilogarithmic paper and the 450 m μ peak recalculated. Then one may rationally proceed to use Liley's graph.

According to Liley, 450 m μ peaks falling in Zone I are associated with Rh negative or mildly affected infants.³ As can be seen from the illustrations, our results are in complete agreement with this. Recently, however, Niswander et al have reported the occurrence of hydrops in association with 450 m μ peaks which are usually seen with mild disease.⁷

Bilirubin peaks falling in Liley's Zone II are more difficult to assess. Here we have relied on serial amniocenteses to help us choose the best time for delivery. Taps were usually repeated at one to three week intervals depending on the height of the initial peak. Shrinking peaks in Zone II have not been associated with severe disease in this series. In these cases, induction has not, as a rule, been considered prior to 36 weeks gestation. Stable or rising peaks were noted to be associated with more serious degrees of erythroblastosis.

Difficulties in interpretation arose in three cases (21, 24, 25) because the initial bilirubin peaks were borderline between Zones II and III. Perhaps amniotic fluid estriol determination would have been helpful in these cases.⁸

Although the series is small, we are encouraged by the overall results achieved in those cases treated by intrauterine transfusion. The technique is not difficult and can be performed effectively in the well-equipped community hospital, whose physicians are motivated to devote the necessary time and effort.

The authors are indebted to the following: Dr. Frederick C. Barald, Department of Radiology, St. Francis Hospital, for his invaluable assistance with the intrauterine transfusions; Dr. Sherwood C. Lewis, who performs all our amniotic fluid analyses; and Mr. Francis J. Sullo, R. B. P., who produced the illustrations for this article.

References

1. Bishop, E. H., Weber, L. L., Israel, S. L.: Intrauterine transfusion. *Am. J. Obst. & Gynec.*, 99, 615, 1967.
2. Bowman, J. M., Pollock, J. M.: Amniotic fluid spectrophotometry and early delivery in the management of erythroblastosis fetalis. *Pediatrics*, 35, 815, 1965.
3. Liley, A. W.: Liquor amnii analysis in the management of the pregnancy complicated by rhesus sensitization. *Am. J. Obst. & Gynec.*, 82, 1359, 1961.
4. Liley, A. W.: Intrauterine transfusion of fetus in hemolytic disease. *Brit. Med. J.* 2, 1707, 1963.
5. Lucey, J. F., in *Intrauterine Transfusion and Erythroblastosis Fetalis*, Report of the Fifty-third Ross Conference on Pediatric Research, Lucey, J. F., and Butterfield, L. J., eds., Columbus, Ross Laboratories, 1966, page 13.
6. Lucey, J. F., in *Intrauterine Transfusion and Erythroblastosis Fetalis*, Report of the Fifty-third Ross Conference on Pediatric Research, Lucey, J. F., and Butterfield, L. J., eds., Columbus, Ross Laboratories, 1966, page 12.
7. Niswander, K. R., Westphal, M. C., and Seekree, S.: Amniocentesis in management of the Rh problem. *Obst. & Gynec.*, 30, 646, 1967.

* General Electric

8. Schindler, A. E., Ratanasopa, V., Lee, T. Y., Herrmann, W. L.: Estriol and Rh isoimmunization: a new approach to the management of severely affected pregnancies. *Obst. & Gynec.*, 29, 625, 1967.

9. Stewart, A. C., and Taylor, W. C.: Amniotic fluid analysis as an aid to the antepartum diagnosis of haemolytic disease. *J. Obst. & Gynec. Brit. Comm.*, 71, 604, 1965.

THE GOLDEN BED

Deeply and instinctively, we think of healing in terms of the bed. Confronted with real illness, our reflex action is to stop the patient working: this gets rid of any ideas he might have had about his personal importance. Then we take away his clothes and put him in a horizontal subservient position: this strips him of his physical dignity, making it clear that he is ill and at our mercy. These reactions date from our impressionable student days, when the ward was presented as the ultimate in the practice of medicine and the consultant envied for his position and opportunities.

The convention holds that there will never be enough beds and that they should never lie empty longer than is necessary to change the sheets. An empty bed stands not for success in emptying but for failure to fill. Despite talk about the dangers of recumbency and of institutionalisation, all my patients are carefully tucked in by tea-time, and early discharge is thought to be full of risk both to the patient and to the bed-occupancy figures. The bed, in fact, is the sacred symbol of medicine. It is put on a pedestal and worshipped not only by those who serve it but by a whole population of believers.

Nearly 35 years of work in hospitals had led me to doubt this simple faith. Not so much for its falsity but because today the bed has been devalued by rapid progress in diagnosis and treatment. Traditional bedside medicine should now be moving into the clinic and the day hospital, and patient care into the patient's home and environment. If each bed were used for its exact purpose we should need fewer. Otherwise there must be a nonmedical element in their use, and (what is worse) a failure to give the patient what he really needs.—Kemp, D.: The Golden Bed. *Lancet* 2: 1025 (Nov. 14) 1964.

Infectious Mononucleosis and Its Relationship to Psychological Malaise

Michael Alfred Peszke, M.D. and William Maxwell Mason, M.A.

There have been two main currents of research in the area of psychosomatic illness. The findings from both schools, while not particularly complementary to each other, are not however contradictory. Canter, Clull and Imboden in a series of predictive studies have pointed up the psychological vulnerability of certain groups of individuals; a vulnerability which manifests itself in prolonged convalescence from infectious illness¹⁻³ or a predisposition to the development of stress induced illness or accident.⁴

On the other hand, a group working at Rochester University, Engel and Schmale have done considerable practical and theoretical work on significant emotional factors in the life span of an individual which may precipitate physiological organic disease.⁵⁻⁸ These workers have postulated that in certain physical illnesses there is a time prior to the development of this illness where a major psychological crisis takes place manifest by such feelings as hopelessness, helplessness and giving up.

In this study we examine and consider the other side of the coin; namely, does a physical illness, in this case infectious mononucleosis, lead to a major psychological disturbance or malfunctioning.

The physiological etiological aspects of infectious mononucleosis are quite outside of the scope of this study, though we are quite assured at this point that it is presumably a viral disease which effects the reticuloendothelial system of the body. For a description of the symptoms, the interested reader is referred to any standard text of medicine. The scope of this study, however, centers on the hypothesis based on clinical speculation that a bout of infectious mononucleosis not always related to the severity of that illness leads to a deterioration in the emotional and psychological functioning of the individual.

In a published study, one that stands alone so far, Greenfield, et al⁹ presented evidence that the length of convalescence from this illness has to do

with the ego strength of the individual. Specifically, the weaker the ego, based on the Barron scale of the MMPI, the longer the convalescence. However, the objective psychological test, the Minnesota Multiphasic Personality Inventory was administered following the illness, and it is hard to know whether one is seeing this as a contaminative of the illness itself.

A thorough test of the linkage between infectious mononucleosis and psychological disorder requires extensive data collection for a large number of individuals. As an initial effort we studied and analyzed the history of the University of Chicago undergraduate class of 1965 (those who entered in 1961) in terms of their use of the Student Mental Hygiene Clinic and extent to which they were tested and examined for potential infectious mononucleosis.

In view of the fact that over this four year period a number of different physicians examined these students and used slightly different criteria for establishing or eliminating the possibility of infectious mononucleosis in their patients, the only workable approach was to use the arbitrary figure of 1/96 of the Heterophile Anti-body (Paul-Bunnell) Test in its unabsorbed form as an indicator of whether the student indeed suffered from this illness. Furthermore, we defined individuals to have had psychological malaise if they at least visited the Student Mental Hygiene Clinic on one occasion. The University of Chicago having an extensive Student Mental Hygiene Clinic, and seeing somewhere in the vicinity of twenty-five percent of its undergraduate body during its four years in college, probably treats or sees the majority of its emotionally disturbed or troubled students, so that the issue of private psychiatrists may probably be discarded.

If, indeed, individuals who contract infectious mononucleosis are more likely to develop some degree of emotional difficulty than those who do not develop that illness then students with the heterophile test values of 1/96 or greater should be most likely to visit the Mental Hygiene Clinic than those whose tests are below that ratio.

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Table I presents the percentages for visiting the Mental Hygiene Clinic divided according to the ratio of the tests and comparing those students to

TABLE I

USE OF THE STUDENT MENTAL HEALTH CLINIC FOR STUDENTS PREVIOUSLY EXAMINED FOR INFECTIOUS MONONUCLEOSIS, AND FOR STUDENTS NEVER EXAMINED FOR INFECTIOUS MONONUCLEOSIS.^a

Test Status	Use of Student Mental Health Clinic		Percentage totals and base N's.
	At least one visit	No visits	
Tested > 1/96	34%	66%	100% (29)
Tested < 1/96	23%	77%	100% (52)
Never tested	27%	73%	100% (469)

Notes:

^a Data source is records of the University of Chicago, Class of 1965. Table N=550, and excludes 23 students who visited the S.M.H.C. prior to being tested for I.M. Class N=573.

those who while having spent four years in college have never been tested even once. It is important to note that this table excludes students who visited the Mental Hygiene Clinic prior to having been tested with a heterophile test for infectious mononucleosis, since these students might well obscure the relationship that we are seeking to demonstrate. It is possible, however, that some of these students may have visited the Mental Hygiene Clinic both before and after the contraction of infectious mononucleosis. However, whatever the reason for these visits, by excluding them we believe that we provide a more stringent test of the hypothesis.

From Table I we see that students who are diagnosed as having infectious mononucleosis by our criteria tend to be more likely to use the Mental Hygiene Clinic, the figures being 37% versus 23%. Comparing these to those students who use the Mental Hygiene Clinic without having been tested we see that they came to 27%. These differences in the use of the Mental Hygiene Clinic find only very modest support in chi square tests of independence. However, the strongest appearing contrast is between the 37% and the 23% which is significant in the 75th percentile of the chi square distribution. We can only say that these data, while not striking, only roughly conform to a hypothesis and are certainly not opposite to the direction hypothesized.

Even, however, if the differences reported in Table I had been more striking this would not in itself have sufficed as a demonstration that infectious mononucleosis leads to psychological malaise.

For it well may be that students with infectious mononucleosis who come to the Mental Hygiene Clinic are already so predisposed by previous psychological difficulties. We, however, have for the Class of 1965 additional information which tends to throw a light on that issue.

As part of their registration as freshmen all students are required to fill out a Cornell Medical Inventory schedule. In this study we used the mental health portion of this schedule (questions 139-195 inclusive) and by scoring affirmative responses to the questions we obtained a rough test of the psychological vulnerability of the student on entrance to college.

If the use of the Mental Hygiene Clinic, in conjunction with a bout of infectious mononucleosis, is due to prior underlying psychological problems then the Cornell scores for this group of students should be higher than those for students who suffer

TABLE II

AVERAGES OF CORNELL MEDICAL INVENTORY SCORES (MENTAL HEALTH SECTION, QUESTIONS 139-195 INCLUSIVE) FOR CLASS OF 1965 ACCORDING TO USE OF THE STUDENT MENTAL HEALTH CLINIC AND I.M. TEST STATUS

Use of the S.M.H.C. ^c	I.M. Test Status		Not tested ^b during 1961-1965
	Tested > 1/96 during 1961-1965	Tested < 1/96 during 1961-1965	
Used S.M.H.C.	2.8 (10) ^a	4.8 (12)	5.6 (30) seen MHC
after testing Did not use S.M.H.C. after testing	2.3 (19)	1.7 (40)	2.9 (23) not seen MHC

Notes:

^a Number in parentheses are the N's over which the averages were computed.

^b Averages for the never tested group are based on a random sample who were present in school 1961-1965.

^c Table excludes twenty-three students who visited S.M.H.C. at least once prior to being tested for I.M.

Statistical Comment:

The data summarized in Table II were subjected to a least-squares multiple classification analysis. The model was additive, with an interaction for students who both had I.M. and visited the S.M.H.C. A small proportion of the variance in the distribution of scores was accounted for by the classification, but the amount is significant at the .05 level. Various alternatives were tried, and various transformations of the scores were also applied. The interaction coefficient was significant regardless of the form of the transformation. Further details are available from the authors.

from infectious mononucleosis but who do not use the Mental Hygiene Clinic. Table II presents the averages and allows a test of this hypothesis.

Table II indicates that students who have used the Mental Hygiene Clinic have on the average higher Cornell Inventory scores than students who did not use the Mental Hygiene Clinic. This gives factual support to the common sense assumption that visiting the Mental Hygiene Clinic is indicative of some psychological difficulty. For our immediate purpose, however, the findings that students who use the Mental Hygiene Clinic after having contracted infectious mononucleosis had Cornell Medical Inventory scores lower than those for students who did not have infectious mononucleosis but who visited the Clinic is significant. The average for the group in question, 2.8 is about as low as for those students who do not use the Clinic at all. These results stand up quite well under statistical scrutiny. Hence, we tentatively conclude that the emotional results of a bout of infectious mononucleosis is not simply a reflection of earlier, underlying psychological difficulty. The data suggests that infectious mononucleosis in itself may precipitate psychological malaise.

Discussion and Summary

We ask whether the contraction of infectious mononucleosis leads to emotional problems. Our data for the University of Chicago Class of 1965 reveals percentage differences in the appropriate direction: Students who contracted infectious mononucleosis were then more likely to use the Mental Hygiene Clinic than those who did not contract infectious mononucleosis or who were not tested for it during their time in college. Unfortunately, the sample is such that it forbids generalizations to a larger population.

Our second hypothesis, independent of the first, demonstrated that students with infectious mononucleosis who sought help for their emotional problems after contracting infectious mononucleosis had underlying premorbid personalities more akin to those who did not have infectious mononucleosis or who were never seen in the Clinic. Because of these findings we reject the hypothesis that being seen in a mental hygiene clinic following infectious mononucleosis is merely the result of the accentuation of previous emotional problems.

Given the crudeness for the data for this analysis and the equivocal support of our first test we cannot claim to have convincingly demonstrated our thesis. A definite result depends on blending of

clinical and statistical approaches with probably more emphasis on the clinical side than was possible with the present retroactive data. Particularly, we recognize the need for more precise and valid measures of emotional crises, psychological health and for the use of the newer diagnostic data on infectious mononucleosis.

Furthermore, the authors are not prepared to speculate at this point on the underlying mechanisms of this tentative correlation. The following, however, should be considered: That a serious bout of infectious mononucleosis by impairing everyday life and routine challenges the psychological defenses, or that by a physiological process certain of the body catechol amines are not as easily detoxified by an affected liver or other reticulo-endothelial systems, and that this leads to a psychophysiological homeostatic imbalance and resulting psychological and functional impairment.

Bibliography

1. Cluff L. E., Canter, A. and Imboden, J. B. "Asian Influenza: Infections, Disease and Psychological Factors." *Archives of Internal Medicine*, Feb. 1966, Vol. 117, pp. 159-163.
2. Imboden, J. B., Canter, A. and Cluff, L. E. "Symptomatic Recovery from Medical Disorders: Influence of Psychological Factors." *J.A.M.A.*, December 30, 1961, Vol. 178, pp. 1182-1184.
3. Imboden, J. B., Canter, A., and Cluff, L. E. "Convalescence from Influenza: Study of Psychological and Clinical Determinants." *Archives of Internal Medicine*, 108; pp. 393-399, Sept. 1961.
4. Canter, A., Imboden, J. B. and Cluff, L. E. "The Frequency of Physical Illness as a Function of Prior Psychological Vulnerability and Contemporary Stress." *Psychosomatic Medicine*, Vol XXVIII, No. 4, Part 1, pp. 344-350. July-August 1966.
5. Adamson, J. D. and Schmale, A. H. "Object Loss, Giving Up, and the Onset of Psychiatric Disease." *Psychosomatic Medicine*, Vol. XXVII, No. 6, pp. 557-576. Nov-Dec 1965.
6. Engle, G. L. and Schmale, A. H. "Psycho-analytic Theory of Somatic Disorder." *Journal of American Psychoanalytic Association*, 15:344, 1967.
7. Schmale, A. H. "Object Loss, 'Giving Up' and Disease Onset" in *Medical Aspects of Stress in the Military Climate*. Walter Reed Army Institute of Research, Washington, D.C. 22-24, April 1964, pp. 433-443.
8. Schmale, A. H. "Relationship of Separation and Depression to Disease." *Psychosomatic Medicine*, Vol. XX, No. 4, pp. 259-277, July-Aug., 1958.
9. Greenfield, N. S., Roessler, R., and Crosby, A. P. "Ego Strength and Length of Recovery from Infectious Mononucleosis." *Journal of Nervous and Mental Diseases*, 129; pp. 125-128, 1959.

Factitious Hyperthyroidism

Report of A Case

F. Patrick McKegney, M.D. and Howard Levitin, M.D.

Although the symptoms of hyperthyroidism are shared by many other syndromes, a careful clinical assessment, together with the wide range of laboratory tests now available, usually leads to satisfactory diagnosis and treatment of the hypermetabolic state. However, certain widely used and misused drugs can either cause signs and symptoms which closely mimic those of hyperthyroidism or may invalidate many of the standard tests of thyroid function.¹ With the increasing amount of medication consumed by Americans, there is a concomitant increase in drug related symptomatology. In those individuals who consciously or unconsciously conceal their use of drugs in doses adequate to cause overt signs of hyperthyroidism, the differential diagnosis and treatment can be very difficult, as the following patient demonstrates.

Case Report

A 26 year old, married housewife was first seen in the Yale-New Haven Medical Clinic in September of 1963, having been referred for "thyroid trouble".

The patient stated that she had been well until 1960, when she had felt a "change in my whole body", following a series of upper respiratory infections, a viral pneumonitis and a severe sinusitis. These illnesses were followed by weakness, easy fatigability, nervousness, irritability, heat intolerance, palpitations, tremulousness and "unusual feelings" in her throat. During this time, she had frequent, irregular and scant menses and a gradual weight loss despite a good appetite. In 1962, the patient's dysphagia had increased to the point where she frequently could only eat baby foods. She first sought medical attention in March of 1963 and a diagnosis of hyperthyroidism was made on the basis of physical examination, including a pulse of 170 and a "borderline elevated PBI". Begun on Lugol's solution for a short period of time, she was switched to 50 mgs. of methimazole daily, without relief of her symptoms, over the next 3 to 4 weeks. She began to complain of diarrhea, 3 or 4 bowel movements a day, increasing protrusion of her eyes, and a total weight loss of 20 pounds prior to her Medical Clinic visit in September, 1963.

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DR. HOWARD LEVITIN, Associate Professor of Medicine, Yale University School of Medicine, New Haven.

Past medical history and review of systems were non-contributory. The patient had been married for 4 years and had been "unable" to become pregnant. There was a questionable history of hypothyroidism and obesity in her mother who had been found to have cancer in September of 1961. Three siblings were alive and well without thyroid disease.

On physical exam, she presented as a short, thin, hyperactive young lady with a stare. Blood pressure was 130/65, a regular pulse of 170, normal respirations and a temperature of 99.8. Her skin was warm and smooth and there was a minimal lid lag without any exophthalmos. The thyroid was neither distinctly palpable nor enlarged and there was no bruit heard. Because of the classic signs and symptoms of hyperthyroidism and a protein-bound iodine of 9.4 gamma %, the patient was begun on Lugol's solution, 5 drops b.i.d., propylthiouracil 100 mg. q6h, and reserpine 0.25 mg. q6h. During the Fall of 1963, there initially seemed to be some improvement, with a four pound weight gain and her pulse dropping to 126. However, she stated that she did not really feel much better. In December, 1963, her pulse was 110 but, because of a protein-bound iodine of 13.1 gamma %, the propylthiouracil was increased to 500 mgs/day. In January, 1964, the patient's status was unchanged and she was admitted to the hospital for a more thorough evaluation of her thyroid status and to establish whether or not the patient was actually taking her medication. Several observers had felt that she showed a "labile personality" and had suggested that perhaps a psychiatric disturbance was responsible for the entire clinical picture.

During her January, 1964 admission, a radioactive iodine study revealed a total 24 hour uptake of less than 1%. Her B.E.I. was 6.6 gamma % and a T3 uptake was "consistent with hyperthyroidism". The patient and her husband were questioned as to either intentional or accidental ingestion of iodine or thyroid containing drugs and this was vehemently denied. The patient was discharged from the hospital on 800 mgs. of propylthiouracil per day but soon thereafter developed a generalized pruritic rash characteristic of a drug eruption. The propylthiouracil was discontinued and she was started on prednisone, 60 mgs/day, which was rapidly tapered over a period of a week to 10 mgs, b.i.d. and methimazole 80 mgs/day was begun. Her acute allergic reaction subsided promptly and since the patient stated that she felt much better, she was continued on methimazole and prednisone for approximately 2 months. However, when the prednisone was discontinued, her original signs and symptoms of hyperthyroidism worsened, in spite of an increase of methimazole to 120 mgs/day.

Since drug therapy apparently was not controlling her symptoms, either because she was taking a thyroid con-

taining medication, and/or because she was refractory to drug therapy, she was readmitted in July, 1964 and all medications were discontinued. On that admission, her physical exam was similar to that in September, 1963. Her initial laboratory studies on the July admission showed a BMR of +25 and an RAI uptake of 0.05% in 24 hours. Three days after admission and without any prescribed drugs, her 24 hour total RAI uptake was 2.8% and a repeat BMR was +37. After the patient had been off of all medication for a week, a third RAI uptake showed a total 24 hour value of 2.5%. Repeated scans of the abdomen to rule out the possibility of ovarian uptake were negative. Despite extensive history-taking and psychiatric consultation, the patient denied ingestion of exogenous agents or of non-prescribed medication either before or during hospitalization and she was supported in this by her husband. Because of the continued suspicion that the patient was ingesting other agents during the July hospitalization, a 24 hour urine collection was quantitatively assayed for amphetamines, which were found at a concentration of 1.1 mg%, and a qualitative analysis showed the presence of a phenothiazine. These findings confirmed that the patient was actually ingesting nonprescribed drugs and a search of her room revealed the presence of many drugs, some of which contained thyroid, atropine, dextroamphetamine and iodine. When the patient was directly confronted with the fact that drugs were in her urine, she continued denying taking the pills. However, when she was told that assistance would be given to help her stop taking the medication, she was very grateful and allowed a more complete search of her room which revealed even more pills of varied types.

Her husband was surprisingly calm when presented with these facts and he acknowledged for the first time that "there were drugs all over the house". The couple agreed to see a psychiatrist following discharge from the hospital but two psychiatric appointments were cancelled by the patient and her husband. When called after the second cancellation, the patient became very angry, claiming she would continue taking the pills because she felt that she "needed them to keep going" and that her husband also refused psychotherapy "because of the cost".

Diagnosis on discharge in July of 1964: 1) Factitious hypermetabolic state secondary to ingestion of desiccated thyroid, dextro-amphetamine and atropine. 2) Immature personality disorder with addictive trends.

Addendum: In July, 1967, three years following our last contact, the patient called her internist (H.L.) and said that she was still feeling very badly and admitted to continued self-medication. Although she agreed to come in with her husband to see the internist, they failed to keep their appointment.

Discussion

This patient presented with classical signs and symptoms of hyperthyroidism, including an onset after an infectious illness and in a setting of marked emotional stress. The early institution of antithyroid medication was prompted by the elevated protein-bound iodine, the tachycardia and the overall acuteness and severity of the hypermetabolic state. A radioactive iodine uptake study was not obtained at that time, although it undoubtedly

would have contributed to an earlier recognition of the actual problem. The uptake would have been low, indicating that the hypermetabolic state was associated with suppression of endogenous thyroid synthesis. This combination of events is seen only with iodine contamination, exogenous thyroid medication or, transiently, with sub-acute thyroiditis at a time when, despite a very low uptake, a fair amount of thyroglobulin is being released into the circulation. This latter condition, however, generally is associated with distinct clinical characteristics not found in the case presented, such as pain, fever and an enlarged thyroid. When the first radioactive iodine uptake was found to be essentially zero, the likelihood of exogenous thyroid intake was immediately investigated, but the vehement denial by the patient and her husband seemed to rule out that possibility. Therefore, treatment efforts directed at an endogenous thyrotoxic state were continued, since thyrotoxicosis refractory to anti-thyroid medication, although not common, is known to occur and has, in addition, been reported in cases without thyromegaly.²

The complex symptomatology observed in this patient was undoubtedly due to the combined effect of thyroid, amphetamine and atropine, causing tachycardia, hyperactivity, weight loss, irritability, etc. Other drugs which have been reported to confuse the laboratory diagnosis of hyperthyroidism are the phenothiazines,^{3, 4} estrogen containing compounds,^{1, 5} and inorganic iodine,^{1, 5} all of which may elevate the protein-bound iodine in an euthyroid patient.

The improvement in the patient's clinical picture when she was put on prednisone for her acute drug reaction to propylthiouracil may have been due to mood elevation or to the known antagonistic effect of steroids on thyroid action.⁶ It is interesting to note that the patient was willing to take the prednisone, which induced a marked clinical improvement in her symptoms, while she also continued to take the agents which caused her original distress. A possible explanation may lie in the fact that the prednisone was prescribed for an allergic rash, a symptom which the patient had not brought upon herself. On the other hand, it may be that the patient was unable to recognize that the multiple drugs she had been taking were causing her distressing symptoms.

The whole issue of this patient's role in her self-induced disease is complex and incompletely understood. Her persistent denial of self-medication, initially strongly corroborated by her husband,

seems to indicate that both of them had a major need for her incapacitating symptoms and continuing medical care. Outlining the "usual" psychological features of patients with self-induced disease is difficult. Such patients may be variously diagnosed as being "psychopaths", "malingerers", "hysterics", or "Munchausens".^{7,8} Determining the particular psychological factors in each case is obviously of great significance for the development of an appropriate treatment plan. In the patient described, for example, less than adequate attention was paid to the husband's role in the problem, with the result that he supported the patient's refusal of psychiatric treatment. For diagnostic purposes, however, certain clinical characteristics, while not specific to factitious illness, are almost always found in such patients, as they were in this case. A complete history, which implies more than casual attention to the family, social and personal background of the patient, should indicate the presence of such characteristics and alert the thorough physician to the possibility of self-induced or, at least, psychogenically determined symptomatology.

These patients usually show indications of unusual dependency and immaturity. As with the case described, they may appear quite childlike, both physically and emotionally, be closely tied to their parents or spouses and rely upon others to take major responsibilities. Our patient did have a job but her work record was spotty. As a potential mother, she admitted having doubts about becoming pregnant and responsible for a child. Her capacity to respond sexually was quite impaired: she had little interest in sex and rare satisfaction with intercourse. As with this patient, factitious symptoms are often used to explain or justify poor personal functioning. Her poor work record, her hesitation to become pregnant and her sexual inadequacies were all presented as resulting from her physical symptoms, without which she said she would be "happy and normal". Indeed, her husband and parents responded to her symptoms and incapacitation with attention and assistance, accepting her as being disabled as a result of a poorly understood physical illness.

Another characteristic of patients with self-induced illnesses is that their physical symptoms tend to occur around life situations which might be expected to cause anxiety, depression or other unpleasant emotions. Patients with factitious illness often do not express and may even deny overt emotional distress about such situations, such as a real or threatened separation from a significant person

in their life. Instead, they complain about their physical symptoms. Our patient became severely symptomatic soon after her marriage, although there were indications that had developed physical symptoms at critical periods in her adolescence and early 20's. Her marriage meant she had to leave home and assume the responsibilities of a wife and homemaker, but she denied any doubts or unhappiness concerning these major changes in her life. Her dysphagia developed and other symptoms worsened when her mother was discovered to have cancer, a fact which she mentioned only incidentally, without apparent concern.

Patients with factitious illness also demonstrate a pattern of inappropriate and contradictory emotional response to their medical care. Our patient demonstrated this pattern when she described her incapacitating symptoms with reactions of detachment, of indifference or, on occasion, of enthusiasm blending into satisfaction. Similarly, she patiently collaborated with the extensive and inconclusive medical workup with little anxiety and even less anger. On the other hand, she easily became irritated and was very demanding about minor issues of nursing care and ward routine.

Finally, although many complaints of patients with self-induced or psychogenic illness may fall within recognizable physiological syndromes, such as hyperthyroidism, a careful history will usually uncover other symptoms or signs which can have little or no possible connection with a single organic etiology. In this regard, Engel⁹ has emphasized the importance of deciding whether a patient's complaints resemble a typical somatic pattern which has a recognizable anatomical and physiological basis; or whether the complaints are "atypical" and described in idiosyncratic terms. In our patient, her stating she felt "a change in my whole body" and "unusual feelings" in her throat were not conclusive but certainly suggestive evidence for a psychogenic etiology. Unfortunately, diseases like hyperthyroidism or syndromes such as the collagenopathies may present such a variety of symptoms that deviations from the "usual" physiologically determined pattern are not easily recognized. In these cases, a conscious effort must be made to obtain data about the patient and his psycho-social situation to "rule in" non-physiological causes for symptoms.

Rather uniquely, the clinical and laboratory diagnosis of hyperthyroidism can be confounded by a patient's ignoring or being unaware of taking an agent which produces a hypermetabolic state.

When the ingestion is consciously concealed, as in our patient, a perplexing situation arises, which requires skillful diagnostic efforts and delicate management by medical and nursing personnel. For example, the discovery of the medication concealed in this patient's room did not assist the medical staff in confronting her with the self-induced hypermetabolic state, since the search and discovery of the pills was done without the patient's knowledge. On the other hand, the laboratory evidence indicating the ingestion of amphetamines and phenothiazines did allow a confrontation with the patient and her husband.

The shift in attitude of both the patient and her husband following this confrontation was rather surprising but probably related to the supportive and helpful attitude of the physicians. The treatment team did not become angry and rejecting, but rather allowed the patient to "save face" and to try and proceed to the next steps of control of self-medication and the acceptance of treatment for the psychological factors causing the ingestion and concealment. In our patient, the shift in emphasis from thyroid to psyche was facilitated because the psychiatrist had been involved early in the diagnostic process, in order to develop a relationship with the patient. That the patient failed to follow the recommended psychotherapeutic program seemed to reflect the same strong need for her symptoms or other effects of the drugs used which had led to the initial denial of self medication. A more intensive and collaborative diagnostic and planning effort, approaching the psychological determinants of her drug abuse during the medical hospitalization, might well have increased the chances of appropriate follow-through by the patient and her husband.

In summary, all patients should be thoroughly evaluated with regard to their personal and social history as well as by physical history, examination and laboratory work-up. This is especially true

when a patient fails to respond to a treatment program appropriate to the medical diagnosis. Those patients who seem to be immature and dependent, whose symptoms show a temporal correlation with life crises and seem to serve as coping mechanisms, and whose attitudes toward their symptoms and incapacitation are unusual or inappropriately comfortable, should be most carefully investigated for a possible psychogenic etiology. Psychological factors may cause symptoms and signs of physical illness in a variety of ways. One of these mechanisms most difficult to diagnose and manage is illustrated by the case of factitious hyperthyroidism presented: a conscious but denied ingestion of pharmacologically active agents which induce phenomena simulating the well recognized organic syndrome. The discrepancies in the laboratory studies are no more important in diagnosis or treatment than is the gathering of data supporting a psychogenic etiology.

References

1. Davis, P. J. Factors Affecting the Determination of the Serum Protein-Bound Iodine, *American J. Med.*, Vol. 40, pp. 918-940, 1966.
2. Weiner, S. C. *The Thyroid*, Harper and Row, 2nd edition. p. 45.
3. Cranswick, E. H.; Simpson, G. H.; and Nies, A. "An Abnormal Thyroid Finding Produced by a Phenothiazine". *J.A.M.A.*, Vol. 181, pp. 554-5, 1962.
4. Oltman, J. E. and Friedman, S. "Protein-Bound Iodine in Patients Receiving Perphenazine". *J.A.M.A.*, Vol. 185, No. 9, August, 1963.
5. College of American Pathology and South Dakota Society of Pathologists. "Serum Protein-Bound Iodine as a Measure of Thyroid Function". *S. Dak. J. Med.* Vol. 19, pp. 31-32, 1966.
6. Werner, S. C. *op. cit.*, p. 673.
7. Asher, R. Munchausen's Syndrome, *Lancet* (1) p. 339, 1951.
8. Bagon, M. Munchausen's Syndrome—Report a Case and Review of the Literature. *Bost. Med. Quart.* Vol. 13, p. 113, 1962.
9. Engel, G. L. "Psychogenic Pain and The Pain-Prone Patient". *Am. J. Med.* June, 1959.

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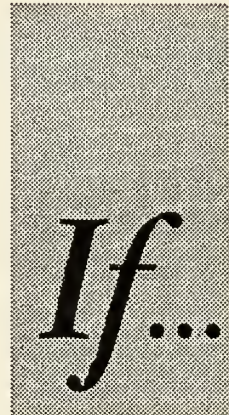
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CALL

ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1969 Annual Meeting of the House of Delegates will be held in the Terrace Room of the Hartford Hilton Hotel, Hartford. The first session of the House of Delegates will commence at 8:30 o'clock in the morning of Tuesday, May 13, with reference committee hearings at 11:45, followed by luncheon. The final session will commence at 8:30 o'clock in the morning of Wednesday, May 14.

Norman H. Gardner, President

Kenneth F. Brandon, Speaker of the House

Frederick C. Weber, Jr., Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society Provides that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates of December 11, 1968 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in *Connecticut Medicine*, "on one or more occasions prior to the next meeting . . . at which meeting the amendment shall be taken off the table and acted upon by the House of Delegates."

Introduced by the Council

I.

ARTICLE VII—Panel on Physician-Hospital Mediation

Purpose: By adopting amendments to the Bylaws which established a Judicial Committee, May 1, 1968, the House of Delegates abolished the need for a "Panel on Physician-Hospital Mediation" since the functions of this panel have been transferred to the Judicial Committee. However, no corollary action was taken to delete the Panel from the Bylaws, and a further amendment is required as follows:

Amendment

ARTICLE VII—The Council

Section 1—Powers and Duties

Par. 12. Special Appointments. (*This paragraph, providing for the election of a Panel on*

Physician-Hospital Mediation and outlining its functions, shall be deleted in its entirety.)

II.

ARTICLE X—Council Committees, Subcommittees, Representatives and Advisors

Purpose: The proposal is made that, with respect to committees, representatives and advisors appointed or elected by the Council, it is neither necessary nor desirable for a listing of such committees, representatives and advisors and definitions of their functions to be made an integral part of the Bylaws. These appointments or elections are made by the Council, from time to time, either by request of an outside agency or on the initiative of the Council, and do not require confirmation by the House of Delegates. Further, when it is evident that one or more of these Council-

elected committees, representatives or advisors have served their purpose and are no longer needed, it should not be necessary to amend the Bylaws (with a 12 month delay) to dissolve or discharge them.

The Council should continue to have the authorization of the House of Delegates to appoint or elect these committees, representatives and advisors. This can be done by replacing the present specific provisions, which include names, functions, etc., with general provisions as outlined below:

Amendment

ARTICLE X—Committees of the Council

Section 1—Council Subcommittees (*Delete entire Section*).

Section 2—Standing Committees of the Council; Paragraphs 1-8 (*Delete entire Section*.)

Section 3—Representatives and Advisors; Paragraphs 1-16 (*Delete entire Section*).

For the three deleted Sections, substitute the following:

ARTICLE X—Committees of the Council

Section 1—Standing Committees, Representatives and Advisors. The Council shall elect or appoint such standing committees, representatives and advisors as may, from time to time, be considered necessary or desirable. Any member of the Society in good standing may be elected or appointed to serve in these posts. The terms of members of standing committees, representatives and advisors shall be set by the Council, but, in any event, shall be reviewed annually by the Council. A current listing of such standing committees, representatives and advisors, including descriptions of the functions of each shall be maintained by the General Manager's office. In its discretion, the Council may dissolve or discharge these standing committees, representatives and advisors in the event that they are no longer necessary or desirable.

Section 2—Council Subcommittees. The Council may, from time to time, appoint ad hoc subcommittees to assist in expediting the business of the Council. Such ad hoc subcommittees shall be appointed from the membership of the Council and all appointments shall be reviewed annually by the Council at its first meet-

ing following the annual meeting of the House of Delegates. Upon completion of their assignments, such ad hoc subcommittees may be discharged by the Council at will.

Section 3* The Judicial Committee. The Judicial Committee shall consist . . . (as adopted by House of Delegates on 5/1/68).

* The election of Judicial Committee members is a "must" function of the Council; it is *not* optional.

III.

ARTICLE XI—Divisional Boards and Committees

Purpose: The Committee on Disaster Medical Care is currently listed under Article X—Committees of the Council under Section 3. Representatives and Advisors, but should have been listed under Standing Committees of the House of Delegates, which this amendment accomplishes.

Amendment

Section 3—Divisional Standing Committees

Par. G. Socio-Environmental Medicine Division
Add: Committee on Disaster Medical Care

Section 5—Duties of Standing Committees

Add new Paragraph 28:

The Council annually shall nominate to the House of Delegates a Committee on Disaster Medical Care, to consist of not less than six members and appoint the chairman thereof. The purposes of this committee shall be to study and keep informed on matters pertaining to the planning of programs designed to provide continuing medical care to the people of Connecticut under disaster conditions; and to cooperate with other agencies in the State engaged in similar activities.

IV.

ARTICLE VII, Section 3—General Manager

Purpose: The Council has approved changing the title of the General Manager to that of "Executive Director", it being found that the latter title is far more appropriate to professional association usage nationwide than is the former.

Amendment

The Council recommends that, *in Article VII, Section 3—General Manager*, and wherever else in the Bylaws the words "General Manager" appear,

these words be deleted and the words "Executive Director" be substituted therefor.

**SUMMARY OF ACTIONS
COUNCIL MEETING**

Wednesday, February 5, 1969

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Dean, Grendon, Weber, Jr., Abbot, Fabro, Bradley, Rogol, Cramer, Farrell, Egan, Petrie, Spitz, Purnell, Shepard, J. M. Grant, Nemoitin, Friedberg, McDonald, R. F. Grant, Pelz, Granoff, Wilson, Palomba and Roch.

Also present were: Mrs. Lindquist, Mr. Villano, Dr. Hess, Dr. Patterson, Mr. Donelan (AMA) and Dr. Richards.

Absent were: Drs. Brandon and Johnson.

II. ROUTINE BUSINESS

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of January 15, 1969.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

- Joseph M. Adzima, Trumbull (FCMA)—1969
- Maxwell J. Antell, Bridgeport (FCMA)—1969
- Carl Bausch, Hartford (HCMA)—1969
- Joseph O. Collins, Watertown (NHCMA)—1970
- Howard S. Colwell, New Haven (NHCMA)1969
- R. Alfred Gandy, Stamford (FCMA)—1969
- Henry M. Glaubman, Hartford (HCMA)—1969
- Isadore S. Goldberg, Torrington (LCMA)—1970
- Gustaf E. Lindskog, New Haven (NHCMA)—1969
- Louis A. Pierson, Meriden (NHCMA)—1969
- Paul D. Rosahn, New Britain (HCMA)—1969
- Jacob A. Segal, Manchester (HCMA)—1969
- Roger C. terKuile, Lebanon, Illinois (FCMA)—1969
- Julius G. Weiner, Hartford (HCMA)—1969

Committee Resignations

- (a) *Conference Committee with Bar Association:*
It was VOTED to accept, with regret, and thank for past service, the resignation of Brae Rafferty, Willimantic, as a member of this Conference Committee.
- (b) *Committee on Program of Scientific Assembly:*
It was VOTED to accept, with regret, the

resignation of Brae Rafferty, Willimantic, as a member of this Committee. Dr. Rafferty's five-year term will not expire until 1970, and he was scheduled to become chairman of the Committee during 1969-70. In order not to disrupt the current five-year terms of the other members of the Committee, it was further VOTED to request the 1968-69 chairman, William F. Eckhardt, Jr., New Canaan, to complete Dr. Rafferty's unexpired term and stay on as chairman for 1969-70. The General Manager was instructed to inform the other members of the Committee of the Council's rationale in taking this action.

- (c) *Committee to Study Perinatal Morbidity and Mortality:* It was VOTED to accept the resignation of Roger K. Gilbert, Waterbury, as a member of this Committee.

Vacancy in Office of CSMS Vice-President

It was VOTED that, in deference to the memory of Max Caplan, Meriden, deceased, the office of CSMS Vice-President, which Dr. Caplan occupied at the time of his death, remain vacant for the balance of the term 1968-69. The Committee on Preliminary Study of Nominations will be instructed to take into account the traditional rotation of the office of President and President-Elect among the County Associations when it meets to prepare a slate of officers for 1969-70; i.e., that it is New Haven County's "turn" to have one of its members nominated for the office of President-Elect in 1969-70.

Interim Appointment of Alternate Delegate to AMA

Having received notice from James M. Grant, Bridgeport, that he is unable to accept the Council's interim appointment (1/15/69) as AMA Alternate Delegate for the balance of the term 1/1/68-12/31/69, it was VOTED to appoint Orvan W. Hess, New Haven, to this post.

Date of Next Meeting

The date of the next Council meeting was set for Thursday, February 27, 1969.

III. OLD, NEW AND SPECIAL BUSINESS

Directive to Committee on Preliminary Study of Nominations

It was VOTED to instruct the Chairman of this Committee (the President) to be prepared to report to the Council, on request, the following information relating to the slate of nominations prepared by the Committee:

- (a) The substance of Committee discussions which had bearing on the selection of particular candidates.
- (b) The tally of votes in cases in which the Committee selected a particular candidate by vote.

Progress Report—CRMP

It was VOTED to accept, with commendation, the report presented by Norman H. Gardner, East Hampton, on the plans and activities of CRMP which are being revised to accommodate to the greatly reduced (from its original request) Federal grant of operating funds for 1969. In essence, Dr. Gardner (a CSMS designate on the CRMP Executive Committee and Advisory Board) indicated that CRMP is "tailoring" its proposed activities during the current year to accommodate to the limited funds awarded to it by the RMP National Advisory Council. Pursuant to this report, the following actions were taken:

- (a) It was VOTED to instruct General Manager to seek to obtain from the Program Coordinator of CRMP a listing of CRMP's current ongoing programs and programs being activated in the near future; also a description of the professional qualifications of CSMS members who CRMP may wish the Council to recommend for service with the several new "Study and Review Committees" that CRMP is reported to be forming.
- (b) It was VOTED to request Dr. Gardner, the CSMS-designate serving on the CRMP Executive Committee, to submit to the Council periodic written reports covering CRMP activities, programs, plans, etc., as such activities, programs, plans, etc. are initiated and/or reviewed by the CRMP Executive Committee and/or Advisory Board.

Report and Recommendation re Voluntary Sterilization

It was VOTED to accept and approve a report filed by the Ad Hoc Committee to Study Abortion, Sterilization and Artificial Insemination on the subject of voluntary sterilization. The report concluded: "We recommend that the Connecticut State Medical Society move to the end that the restrictions and the administrative limitations on voluntary sterilization be removed (by appropriate legislative action) and that the individual be given the right to decide with his or her physician on the personal indications for sterilization".

Dr. Friedberg, Chairman of the Committee on State Legislation, reported that but one bill on this question had come to his Committee's attention thus far (H.B. 5411), and that in his Committee's view, that bill was so vague and poorly written that it would not serve the purposes stated in the Ad Hoc Committee's report which had just been approved by the Council. In addition, some members of the Council expressed the opinion that the Ad Hoc Committee's recommendation was too broad and all-inclusive, and that a number of moral, medical and legal questions which might be raised by the performance of sterilization ought to receive appropriate attention before the Society committed itself completely on this subject. However, no action was taken which called for further study to be made.

COMPAC

It was VOTED to request the Chairman to appoint an ad hoc committee to study and report on the following:

1. A letter from the COMPAC Board of Directors which poses a number of questions to the Council concerning COMPAC's future operations and its relationship to the Society; and
2. A resolution received from the Board of Directors of the Hartford County Medical Association which makes several recommendations concerning the transferral to the Society certain functions now being carried on by COMPAC and a change in the existing relationship between COMPAC and the Society.

The Chairman appointed the Ad Hoc Committee as follows:

- Morris A. Granoff, New Haven, Chairman
- Sidney L. Cramer, Hartford
- E. Tremain Bradley, Norwalk

- (a) It was VOTED to refer to the same Ad Hoc Committee, for prompt study and implementation, a portion of the letter from the COMPAC Board (see 1. above) which proposed that the Council arrange and hold a Conference of County Medical Association Officers, if possible, prior to the first of the County Association annual meetings this spring, the theme of such Conference to be medical political education and action and the AMPAC-State PAC operation and objectives. It was further VOTED to authorize the Ad Hoc Committee to request COMPAC to develop and arrange for speakers for the program, and to share jointly with the Society the costs of the Con-

ference; also, that the CSMS staff be authorized to pay whatever share of the costs that is recommended by the Ad Hoc Committee.

"Usual and Customary Charges" vs. "Fee Schedules"

(a) It was VOTED to accept, with commendation, a verbal report presented by several members of the Council on the discussion they had with Insurance Commissioner Cotter at his office on January 20, 1969. In brief, the members reported that they had presented the Commissioner with a staff analysis of the listing of "doctors" that had signed to participate in the CMS Century Contract, the listing having been furnished by the Commissioner, on which he had based his opinion that "60% of Connecticut physicians" had so signed. He agreed that 1142 M.D.'s engaged in patient care in Connecticut do not constitute more than 25-30% of all those eligible, but stated that his estimate had been based on a comparison of 1442 M.D.'s who had signed with a list of 2400 M.D.'s who had received payments from CMS in 1967, under the Preferred and/or Community Contracts. Pursuant to the acceptance of this verbal report, it was VOTED to convey to Commissioner Cotter the sincere thanks of the Council for having furnished the aforementioned list to the Society, and for having granted an audience to CSMS representatives to discuss this and related matters. It was further VOTED to direct the Committee on State Legislation to attempt to get a "committee bill" before the General Assembly in the 1969 session which would require that the Insurance Commissioner receive documented evidence that at least 50% of M.D.'s licensed and residing in Connecticut had signed to participate in any new medical service corporation contract which offered full-pay coverage to subscribers, before the Commissioner could approve such contract in the future.

Finally, it was VOTED to urge Commissioner Cotter to implement a proposal discussed at the meeting to require CMS to inform potential purchasers of the Century Contract what percentage of physicians have signed to participate and accept in-full payments in the area in which enrolled subscribers will obtain their medical care services.

Legislative Roundup

Isadore H. Friedberg, Chairman of the Committee on State Legislation, brought the Council up

to data on the status of bills sponsored by the Society and a number of other bills that have bearing on health and/or medical care.

Based on this report, it was VOTED to refer a bill concerning the licensure of psychologists to the Committee on Mental Health for opinion, and to request Charles Polivy, Hartford and Sidney L. Cramer, Hartford, to represent the Society at hearings and other legislative functions to speak in support of the "usual, customary and reasonable charge" concept and its continuance under Medicaid.

Treatise on "Legal Relationship of Physician to Hospital"

Having acted to receive this treatise, prepared by J. Alfred Fabro, "as information" on January 15, 1969, it was now VOTED to accept the treatise and authorize its distribution to the AMA Delegates, Alternate AMA Delegates and Executive Secretaries of the other five New England State Medical Societies.

Communication—Medical Staff of St. Vincent's Hospital (Bridgeport)

It was VOTED to receive, with thanks, notice of the adoption by the Medical Staff of St. Vincent's Hospital of a resolution affirming support of the CSMS Council's position that the Society not give full approval to the Connecticut Regional Medical Program until CRMP authorizes a much greater representation of practicing physicians on the CRMP Advisory Board and Executive Committee. The Council advocates that "at least one-third" of the Advisory Board members be practicing physicians, with "equivalent" representation on the Executive Committee. It was further VOTED to apprise the officers of the component County Medical Associations of this action by the St. Vincent's Hospital Staff and to urge that efforts be made at the county level to gain support for the Council's subject position by hospital staffs within each county's jurisdiction. The chiefs of staff of all Connecticut hospitals have received notice of the St. Vincent's Staff action.

Report—Committee on Postgraduate Education

Based on the report of Arthur Ebbert, Jr., on the proceedings of the AMA Conference on Continuing Medical Education (received as information by the Council on 1/15/69) actions were taken on three recommendations of this Committee as follows:

1. It was VOTED to approve the concept of the AMA award program for physicians who par-

ticipate in continuing medical education in accordance with AMA criteria.

2. It was VOTED to authorize the Committee to transmit to the new AMA Department on Continuing Medical Education the "reservations" the Committee has regarding the methodology AMA is currently proposing for implementing the awards program (see 1 above).
3. It was VOTED to implement a recommendation of the Committee that the "thinking" on medical education at the grass roots level be obtained to guide the Committee's efforts toward "extending, promoting and disseminating continuing education to all physicians in the state" by authorizing the holding of a County Medical Association Officers Conference on this and related subjects, the program for such Conference to be arranged by the Committee on Postgraduate Education.

Release of Medicaid Information by Welfare Department

It was VOTED to receive as information a report made by the General Manager concerning the January 30, 1969 ruling of the State's Attorney General that the "right to know" statutes require that the Commissioner of Welfare release the names of physicians receiving payment for services rendered to Medicaid beneficiaries and the amount of payments made to each; further, that Commissioner Shapiro would hold a press conference on Friday, February 7, at which these names and amounts would be made public; and, finally, that a statement defining the Society's position in this matter had been mailed out to the communications media on Wednesday, February 5th (the day of the Council meeting). It was understood that Charles Polivy, Hartford, Chairman of the Title XIX Medical Advisory Committee, other members of the MAC, President Gardner of CSMS, and the General Manager had been invited to attend and participate in the press conference called by the Commissioner.

SUMMARY OF ACTIONS COUNCIL MEETING Thursday, February 27, 1969

I. ATTENDANCE

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Grendon, Brandon, Abbot, Fabo, Bradley, Rogol, Cramer, Egan, Spitz, Purnell, Nemoitin, Friedberg, Johnson, McDonald, R. F. Grant, Pelz, Granoff, Palomba and Roch.

Also present were: Mrs. Lindquist, Dr. Hess, Dr. Patterson, Mr. Donelan (AMA), Mr. Villano and Dr. Richards.

Absent were: Drs. Dean, Farrell, Petrie, Shepard, J. M. Grant and Wilson.

II. ROUTINE BUSINESS

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of February 5, 1969.

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Edmund Beizer, Hartford (CHMA)—1969
B. Bayliss Earle, Glastonbury (HCMA)—1969
Bernard C. Peck, New Britain (HCMA)—1969
Charles N. Sullivan, New Britain (HCMA)—1969
Alexander J. Tuttle, Hartford (HCMA)—1969

Election of Student Member

It was VOTED to elect to Student Membership the following Connecticut resident who is attending the medical school indicated:

Leonard H. Alberts, 50 Iroquois Rd., West Hartford
New York Medical College—1972
Pre-Med: Miami University of Ohio
Parent: Manuel M. Alberts

Date of Next Meeting

The date of the next meeting was set for Wednesday, March 19, 1969, the time of the meeting to be determined by the Chairman. A Conference of County Medical Association Officers will follow at 4:00 P.M., which suggests that the Council meeting will start at 12:00 P.M. or earlier.

III. OLD, NEW AND SPECIAL BUSINESS

Report—Section on Ophthalmology

It was VOTED to accept the recommendation of the Section that "the CSMS Committee on Eye Care should continue to function in its present form".

Report—Judicial Committee re Relations with Chiropractors

It was VOTED to approve the report of the Judicial Committee on the relation of physicians with chiropractors as follows:

1. It is unethical for an M.D. to refer medical problems to a chiropractors.

2. Any referral of a medical problem by a chiropractor to an M.D. shall be treated by the M.D. as a referral of a medical problem from a lay person.
3. It is unethical for a radiologist to accept any referral from a chiropractor for his services. He may not send any reports to a chiropractor, even if requested to do so by the patient.

This action of the Council makes these rules of ethics binding on all members of the Society. They will be published in the Journal and given prominent display.

Report—Judicial Committee re Medical Credit Card Systems

It was VOTED to approve the report of the Judicial Committee on medical credit card systems as follows:

The use of medical credit cards is considered *not* to be in the best interests of patients and *not* in conformance with high professional standards.

It was further VOTED that, after any existing contracts with any medical credit card agency expire, neither the Society nor any of its component County Associations encourage medical credit card plans by permitting their advertisement in the Journal or other medical publication, or use of membership mailing lists, or rental of space for exhibits at meetings.

Report—Judicial Committee re Uniform Anatomical Gift Act

It was VOTED to approve the report of the Judicial Committee on this subject as follows:

That the Society support SB 935, introduced by Senator Jay Jackson, 5th District, which embodies the "Uniform Anatomical Gift Act" (AMA-ABA) and an added section which establishes the criteria to be met by a physician declaring a patient (donor) to be dead.

Report—Judicial Committee re Publishing Disciplinary Actions

It was VOTED to refer back to the Judicial Committee, for further study, a report on the question of publishing in the Journal disciplinary actions imposed on CSMS members by the Connecticut Medical Examining Board. Such "further study" is to include consultation with the CMEB concerning the subject question and also exploration of the possibility of establishing continuing liaison between the CMEB and the Judicial Committee.

Report—Judicial Committee re Pre-Signed Prescription Blanks

It was VOTED to approve the report of the Judicial Committee on this subject as follows:

The practice of pre-signing prescription blanks to be left at pharmacies, nursing homes, hospitals and similar places shall be considered both unethical and unprofessional conduct on the part of the physician.

This action by the Council makes this rule of ethics binding on all members of the Society. It will be published in the Journal and given prominent display.

In a related action, it was VOTED to publish notice in the Journal also, for the information of members, that being found guilty of such unethical and unprofessional conduct can lead to action by the Connecticut Medical Examining Board which may suspend or revoke the physician's license to practice.

Report—Judicial Committee re Principles of Cooperation with Attorneys

It was VOTED to approve the report of the Judicial Committee on this subject as follows:

That the Council accept the text of the proposed revision of the "Medico-Legal Guide—Principles of Cooperation" for the purpose of expediting better relations between the medical and legal professions, with the understanding that the principles will be reviewed within a reasonable period of time for possible amendment. In taking this action, it was acknowledged that some members of both the Council and the Judicial Committee are not completely satisfied with the wording of several sections of the document. Nevertheless, the action has the effect of making the "principles" binding on all members of the Society and infractions thereof subject to disciplinary action.

Rather than publishing the revised version in booklet form at this time, the "Principles" will be published in *Connecticut Medicine* for the information of CSMS members and reprints will be offered to the Connecticut Bar Association for distribution to its members.

Report—Committee on Preliminary Study of Nominations

The Committee presented to the Council a complete slate of nominees for officer and committee posts for election in 1969. After making a few changes in the nominations for the various committee rosters, the Council VOTED to approve these and transmit them to the House of Delegates for election at the 1969 Annual Meeting.

Concerning the slate of officers presented by the Committee, several additional nominations for several of the posts were made from the floor and a vote was taken in each case by secret written bal-

lot. As approved by the Council, the slate to be presented to the House of Delegates is as follows:

For President: Stevens J. Martin, Hartford
(without election)

For President-Elect: Morris A. Granoff, New Haven

For Vice-President: Louis Rogol, Danbury

For Secretary: Reginald C. Edson, West Hartford

For Treasurer: David A. Grendon, Sharon

For Speaker: Kenneth F. Brandon, Hartford

For Vice-Speaker: Frank K. Abbot, Waterbury

For AMA Delegate: Norman H. Gardner, East Hampton (Term: 1/1/70-12/31/71)

For Alternate AMA Delegate: Orvan W. Hess, New Haven (Term: 1/1/70-12/31/71)

For Councilor-At-Large: Charles Polivy, Hartford

Having learned that Bernard F. Mann, Jr., New Haven, has requested that he be relieved of the chairmanship and membership on the Committee on Health Careers, it was VOTED to commend Dr. Mann for his many years of outstanding service as the Committee chairman and to convey the Council's appreciation for same to him. The Committee on Preliminary Study of Nominations suggested that the Council might wish to study the question of limiting tenure of office with respect to membership on committees, serving as representatives and advisors, etc. However, the Council took no action in this suggestion at this time.

Report—Ad Hoc Committee on Contacting HEW Secretary

It was VOTED to approve the report and recommendation of the Ad Hoc Committee as follows: That the President, President-Elect and Immediate Past President constitute a CSMS "task force" to meet with the new HEW Secretary, Mr. Robert Finch, for the purpose of conveying to him the grass roots socio-economic opinions of the medical profession in Connecticut and of leaving with him such published policies of the Society as may be pertinent. Arrangements for the meeting are to be made, if possible, by Rep. Thomas Meskill of Connecticut in cooperation with the AMA's Washington office. The "task force" membership: Drs. Norman H. Gardner, Stevens J. Martin and E. Tremain Bradley. In accordance with the Ad Hoc Committee's recommendation, the meeting will be scheduled for the earliest mutually agreeable time possible.

Report—Committee on Public Health

It was VOTED to accept as information a report filed by this Committee which covered the following:

(a) *Measles*

RESOLVED: That the Council of the Connecticut State Medical Society go on record as stating that it is important that as many children as possible should receive immunization against measles; and be it further

RESOLVED: That the Council recommend especially such immunizations be given in all Well-Child Clinics and private physicians' offices, and be given to all children before school entrance.

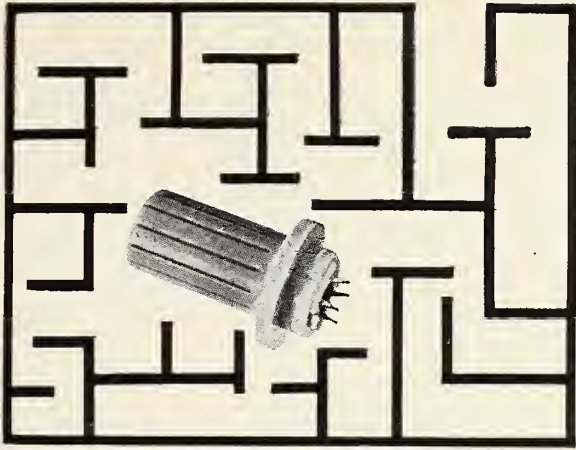
(b) *Program for Prevention of Erythroblastosis by Vaccination.* The Committee favors this program and recommends its continuing evaluation.

Report—Welfare Commissioner's Release of Medicaid Information

It was VOTED to receive as information a verbal report presented by the General Manager on the the proceedings of the February 7 press conference at which Commissioner Shapiro released to the communications media the 1967 statistics of payments made for physicians' services under Medicaid; i.e., the names of all physicians who had received \$2500 or more in 1967, and the total amount paid to each. It was the General Manager's opinion that the entire session, and the publicity which surrounded it, was unnecessarily embarrassing to physicians who had participated in the Medicaid program, since nothing of any real consequence was brought to light by the release of the information or the question and answer period which followed.

Progress Report—Status of "Usual and Customary Charges" Under Medicaid

Drs. Gardner, Cramer and Richards reported on the hearing of the Assembly's Committee on Public Welfare and Humane Institutions (2/24/69) at which the Society's two bills (SB 573 and SB 574) on continuing the "usual and customary charge" program for physicians beyond March 1, 1969 were heard. No one appeared to testify in opposition to either bill, or to bills which would provide "usual and customary" programs for dentists, chiropodists and optometrists (as approved by the Title XIX Professional Advisory Committee). However, the press reported subsequently that the co-chairmen of the Committee had stated that they had no intention of acting on either SB 573 or SB 574 until later on in the legislative session. This means (as




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Commissioner Shapiro testified) that the method of paying physicians from March 1st until the Assembly took some positive action will be left in "limbo" as far as the Welfare Department is concerned.

Dr. Cramer reported that the Title XIX Professional Advisory Committee, on which he serves as a CSMS representative, met on February 27th and voted to transmit a recommendation to the leadership of the Assembly (President Pro Tem of the Senate) and the co-chairmen of the Committee on Public Welfare and Humane Institutions that "no change in the usual and customary program under P.A. 548 be instituted until such time as the General Assembly acts to create new legislation" and that "the Committee be asked to report out favorably on SB 573 immediately with the effective date of the act to be March 1, 1969".

N.B.: Apparently the recommendation of the PAC and all other supporters of continuing "usual and customary" fell on deaf ears among the legislators concerned since no action was taken on SB 573 and the program went out of existence at midnight on February 28th. An emergency "fee schedule" has been constructed jointly by the Commissioner of Welfare and the Commissioner of Finance and Control which, apparently, will remain in effect until the General Assembly gets around to taking some definitive action on the basic question of continuing "usual and customary".

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on February 5, 1969 and February 27, 1969. Detailed minutes of the meetings are on file at 160 St. Roman Street, New Haven, for perusal by and interested member of the Society.*

Placement Wanted

PATHOLOGIST—Age 43, Board certified A.P.-C.P. wishes partnership or associate position in a smaller hospital in N.E. or Central Connecticut preferably. Connecticut license.

INTERNIST—33, Board eligible, subspecialty in Rheumatology, Connecticut license. Desires to locate in Connecticut and interest in practice in either association, group, hospital, student or employee health. Available Summer 1969.

GENERALIST—Age 62, desires position in Connecticut full time, 40 hours per week in hospital or emergency room service, or employees' clinic in industry. Connecticut license.

Placement Opportunities

PRACTICE FOR SALE—Well-established practice in Internal Medicine available. Modern offices and laboratory, large practice. New Haven County.

PSYCHIATRIST—Community-oriented mental hospital, to work in or direct a 500-bed comprehensive mental health center, one of several units in a 1600-bed hospital. Opportunity for teaching, clinical work and research, also to work with or direct a team of social workers, psychiatric residents, psychologists, occupational therapists and approximately 190 nursing staff personnel. Opportunity for association with Wesleyan University, Yale and UConn. Qualified candidates may be considered for other senior staff positions. Liberal benefits with housing available at a nominal charge, annual leave to attend medical conventions. Send all particulars in first letter, including references, to Mehadin K. Araleh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

SENIOR STAFF PSYCHIATRIST—full time, residential psychiatric rehabilitation center, 40 miles from New York City, in desirable living area with good schools. Non-profit Foundation oriented to intensive, individualized, eclectic psychotherapy. Large out-patient service also. Salary open, dependent upon experience. Benefits include major medical insurance, life insurance and pension program. For information, write: Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

PEDIATRICIAN—for a rapidly growing community in Western Connecticut. Present pediatrician wants to concentrate solely on subspecialty. Arrangement on solo, salary or associate basis.

OBS-GYN—Board certified OB-GYN desires certified or qualified associate for practice in small eastern Connecticut town. Contact: Edmond B. Raheb, M.D., 14 Carter Street Danielson, Connecticut 06239.

EDUCATIONAL OPPORTUNITY—PSYCHIATRIC RESIDENCIES available in a community-oriented mental hospital. Comprehensive treatment facility for central Connecticut. Associated with Yale Departments of Psychiatry and Neurology which provides supervision and opportunities for

(Continued on page 285)

Behavioral Toxicity of Psychotropic Drugs:

V. Effects on Gross Behavior Patterns

Alberto DiMascio, Ph.D., Richard I. Shader, M.D.
and Gerold S. Harmatz, A.B.

In the second article of this series,^{1, 2} two types of mood changes were described ("paradoxical" and "pendular") that could be considered as adverse drug induced effects. "*Paradoxical*" effects are those alterations in mood in a direction opposite to the "clinically desirable" one for which the drug has been prescribed. "*Pendular*" effects are those alterations that proceed in the "desired" direction to the degree that the resultant mood tends towards the opposite state for which the drug was initially administered.

"Paradoxical" and "pendular" drug induced changes are not limited to just single mood states, similar alterations in the gross behavior pattern also occur.

The anti-psychotic drugs have "*paradoxically*" induced acute psychotic reactions marked by confusion, incoherent rambling, disorientation, paranoid ideation, increased agitation and excitement, violent maniacal behavior, visual and auditory hallucinations or by depersonalization.³⁻⁹ It has been suggested that these phenomena are merely the uncovering of latent schizophrenic symptoms, but others argue against this view since they cite cases showing that they appear in previously non-psychotic individuals.⁸⁻¹²

"*Pendular*" changes in gross behavior patterns have been reported to occur as consequences of the motor-inhibiting and mood-suppressing actions of anti-psychotic drugs. Phenothiazines have induced

in acutely disturbed and agitated patients catatonic-like states (muteness, immobility, increased salivation, and negativism);¹³ and depressive states have been "precipitated by phenothiazine"¹⁴—states characterized by motor retardation, despair, sexual disinterest, insomnia, guilt feelings, and a disinclination to live.

The previously mentioned psychodynamically-oriented hypotheses of Sarwer-Foner,¹⁵ Azima,¹⁶ and Klerman and DiMascio,¹⁷ also have been used to explain the "paradoxical drug effects" on gross behavior. May,¹³ on the other hand, utilized a biochemical model in proposing that the catatonic-like states occur by ". . . blockage of the ergotropic system through interfering with the action of brain norepinephrine, resulting in a preponderance of the trophotropic division with increased liberation of 5-hydroxytryptamine." There is insufficient evidence to substantiate either of these proposals.

"*Pendular*" effects after antidepressant agents on gross behavior patterns have also been noted. The mood-elevating and stimulant properties of these drugs have resulted in retarded depressed patients passing through the desired state and becoming (in a "pendular" action) euphoric, hypomanic, outwardly hostile, talkative or with flight of ideas after imipramine,¹⁸⁻²¹ nortriptyline,^{22, 23} and MAO inhibitors—including phenelzine, nialamide and tranylcypromine.²⁴⁻³³

"*Paradoxical*" effects are gross behavior—in the sense that the term has been used in this review—have not been reported after antidepressants. That is, no one has published data from which the conclusion could be drawn that a deepening of the depressive syndrome was the direct result of antidepressant medication. What has been reported, and called "*paradoxical*"—although it really could more descriptively be labelled "*atypical or unexpected*"—is the capacity of antidepressants to induce or uncover psychotic reactions—manifested by confusion, thought disorganization, disorientation,

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GEROLD S. HARMATZ, A. B., Senior Research Assistant, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, and Harvard Medical School.

visual and auditory hallucinations, distortion of preception, or depersonalization, as well as the concomitant affect changes. These reactions have been noted after imipramine,^{19-21, 34-39} amitriptyline,⁴⁰ and after the MAO inhibitors, tranylcypromine and phenelzine.^{30, 41-43}

Berthiaume,²⁰ showed the above phenomena as generally resulting from the fact that the drugs cause a disappearance of the inhibiting depressive element and, hence, allow the underlying schizophrenic psychopathology to appear. Klein,¹⁹ also concluded that the psychogenic action of imipramine "occurs only in the presence of psychotic or CNS pathology." He presented a two-stage cybernetic model involving activating systems to explain the exacerbation of psychosis produced by imipramine. Both Ayd,²⁸ and Hudgens,⁴⁰ however, present cases in which there was no history of bizarre psychiatric symptoms and in whom cessation of the drug produced a rapid remission of such symptoms. Thus, both the "uncovering" and "production" of psychotic symptoms have been attributed to antidepressant drugs. Klein,³⁶ further proposed an organic CNS predisposition to explain the visual hallucinations with imipramine. (We would like to remind the readers that in this review, we have referred only to those articles in which drugs were used within the "usual" dosage range. Phenomena resulting from gross overdosage were not included. For pragmatic reasons, we could not delve into the matter of individual dosage thresholds, although some may argue that the above symptoms could be explained by stating that, whatever the dose administered, it was an overdosage for that particular individual. Rikovsky,³⁴ cites a number of investigators who believe that these phenomena occur only in older patients, or in patients with a high dosage administration; however, his own data do not support these contentions.)

"Atypical" effects on gross behavior also have been reported after antianxiety agents. Mayler,²² indicated that paranoid features and Korsakoff-like psychoses have been reported after chlordiazepoxide. Ayd,⁴⁴ cited examples of confusional states, maniacal reactions with garrulousness and intoxication feelings occurring after chlordiazepoxide. Dickel and Dixon,⁴⁵ reported acute manic reactions after meprobamate, and Beric,⁴⁶ reported agitation, excitement, insomnia and aggravation of existing neurotic manifestations with meprobamate. In addition, there have been reports of vivid bizarre dreams and nightmares with chlordiazepoxide^{47, 48} and diazepam,⁴⁹ they were perceived

so dramatically with chlordiazepoxide that termination of the drug was necessary.

The impression is gained in reading the literature that these drug induced "behavioral side-effects" are relatively rare and unexpected sequelae of drug administrations. The probability is, however, that these drug actions are really neither as rare nor as unexpected as the literature would have one believe. A number of reasons exist that lead us to make this statement. First among them, is the fact that the definition of what constitutes, or what is to be included under the term, "behavioral toxicity" has never really been clearly set down.

Second, is that the symptom complex of what may be considered as "behavioral toxicity" is so highly intertwined with the clinical status of the patient, and changes therein, that it has been difficult to recognize and isolate them as being a resultant of drug administration. This difficulty is underscored when one considers the frequent non-correspondence of self and observer reports of behavioral changes.⁵⁰ Further, in instances where group data and objective methods for quantifying drug actions are used, the statistical procedure of reporting results as group averages often obscures bidirectional changes and the extreme responses; the extreme "positive" responses may be mentioned, the extreme "negative or adverse" ones seldom mentioned.

Regardless of the frequency of such effects, the disastrous consequences of these reactions—both therapeutically and potentially to the health of the patient—are such that they demand increased awareness of the phenomena and more extensive investigation aimed at explaining these reactions—if they are to be avoided.

References

1. DiMascio, A., Shader, R. I.: Behavioral Toxicity of Psychotropic Drugs: I Definition, *Conn. Med.* 32: 617-620.
2. DiMascio, A., Shader, R. I.: Behavioral Toxicity of Psychotropic Drugs: II Toxic Effects on Psychomotor Functions, *Conn. Med.* 32: 617-620, 1968.
3. Malitz, S., Houch, P. H., and Lasse, S.: A two-year Evaluation of Chlorpromazine in Clinical Research and Practice, *Amer J Psychiat* 113: 540, 1956.
4. Chaffin, D. S.: Phenothiazine-Induced Acute Psychotic Reaction: The "Psychotoxicity" of a Drug, *Amer J Psychiat* 121: 26, 1964.
5. Sarwer-Foner, G. J., Grauer, H., MacKay, J., and Koranyi, E. K.: Depressive States and Drugs: A Study of the Use of Imipramine "Tofranil" in Open Psychiatric Settings, *Med Serv J* 15: 359, 1959.
6. Hafner, H., Hayder, B., and Kutscher, I.: Undesirable Side-Effects and Complications with the Use of Neuroleptic Drugs, *Int J Neuropsychiat* 1: 46, 1965.

7. Lang, A. E., Moore, R. A.: Acute Toxic Psychosis Concurrent with Phenothiazine Therapy, *Am J Psychiat* 117: 939, 1961.
8. Sher, N.: Hallucinations after Chlorpromazine in an Otosclerotic, *Am J Psychiat* 118: 746, 1962.
9. Hollister, L. E.: Complications from the Use of Tranquilizing Drugs, *N E J Med* 257: 170, 1957.
10. Hollister, L. E.: Human Pharmacology of Anti psychotic and Anti depressant Drugs, *Ann Rev Pharm* 8: 491-516, 1968.
11. Schroeder, H. A., Perry, H. M.: Psychosis Apparently Produced by Reserpine, *J A M A* 159: 839, 1955.
12. Von Loffler, W., Essellier, A. F., Prott, F., and Wagmann, A.: Hochdruckbehandlung mit eninam Rauwolfiaalkaloid (Serpasil): Klinische Bsbachtungun, *Schweizerische Medizinische Wochenschrift* 83: 1012, 1953.
13. May, R. H.: Catatonic-Like States Following Phenothiazine Therapy, *Am J Psychiat* 115: 1119, 1959.
14. Simonson, M.: Phenothiazine Depressive Reaction, *J Neuropsychiat* 2: 259, 1963.
15. Sarwer-Foner, G. J.: Recognition and Management of Drug-Induced Extra-Pyramidal Reactions and "Paradoxical" Behavioral Reactions in Psychiatry, *Canad Med Assoc J* 83: 312, 1960.
16. Azima, H., and Sarwer-Foner, G. J.: Psychoanalytic Formulations of the Effects of Drugs in Pharmacotherapy, in *Extra-Pyramidal Systems and Neuroleptics*, J. Bordeleau (ed.), Montreal: Revue Canadienne de Biologie, 1961, p. 507.
17. Klerman, G. L., DiMascio, A., Rinkel, M., and Greenblatt, M.: The Influence of Specific Personality Patterns on the Reactions to Phrenotropic Agents, in *Biological Psychiatry* (Vol. I), J. Masserman (ed.), New York, Grune & Stratton, 1959, p. 224.
18. Bruna, G. G., Himwich, H. E.: Biogenic Amines and Behavior in Schizophrenic Patients, in *Recent Advances in Biological Psychiatry* (Vol. 5), J. Wortis, (ed.), New York: Plenum Press, 1963, p. 144.
19. Klein, D. F.: Behavioral Effects of Imipramine and Phenothiazines; Implications for a Psychitric Pathogenetic Theory and Theory of Drug Action, in *Recent Advances in Biological Psychiatry*, (Vol. 7), J. Wortis, (ed.), New York: Plenum Press, 1965, p. 273.
20. Berthiaume, M.: Alteration of the Clinical Picture During Tofranil Therapy, *Canad Psychiat Assoc J (Suppl)* 4: 187, 1959.
21. Hohn, R., Gross, G. M., Gross, M., Lasagna, L.: A Double-Blind Comparison of Placebo and Imipramine in the Treatment of Depressed Patients in a State Hospital, *J Psychiat Res* 1: 76, 1961.
22. Mayler, L.: *Side-Effects of Drugs: Adverse Reactions as Reported by the Medical Literature of the World 1963-1965* (Vol. 5), New York: Excerpta Medica Foundation, 1966, p. 16.
23. Bennett, I. F.: The constellations of Depression: Its Treatment with Nortripyline. II. Clinical Evaluation of Nortripyline, *J Nerv Ment Dis* 135: 59, 1962.
24. Goldberg, L. I. Monoamine Oxidase Inhibitors, *J A M A* 190: 456, 1964.
25. Cares, R. M., Buckman, C.: A Survey of Side-Effects and/or Toxicity of Newer Psychopharmacologic Agents, *Dis Nerv Sys* 22: 97, 1961.
26. Johnson, J., and Eilenberg, M. D.: Psychotic Reactions and Phenelzine (Mardil), *Brit Med J* 2: 857, 1960.
27. Cole, R. A., and Weiner, M. F.: Clinical and Theoretical Observations on Phenelzine (Mardil), An Anti-Depressant Agent, *Am J Psychiat* 117: 361, 1960.
28. Ayd, F. J.: Psychopathic Reactions to Anti Depressant Drugs, *J Neuropsychiat* 2: 119, 1961.
29. Sarwer-Foner, G. J., Koranyi, E. K., Meszaros, A., Grauer, H.: Depressive States and Drugs. II. The Study of Phenelzine Dihydrogen Sulfate (Nardil) in Open Psychiatric Settings, *Canad Med Assoc J* 81: 991, 1959.
30. Kruse, W., Hoermann, M. G.: Clinical Evaluation of Four Anti-Depressant Drugs, *Curr Therap Res* 2: 111, 1960.
31. Imlah, N. W.: Overshotting Action of Phenelzine, *Lancet* 1: 826, 1960.
32. Atkinson, R. M., Ditman, K. S.: Tranlycypromine: A Review, *Clin Pharmacol Ther* 6: 631, 1965.
33. Chu, J., Fogel, E. J.: Clinical Evaluation of the Thy-moleptic Effect of Tranlycypromine, *J Indiana State Med Assoc* 56: 40, 1962.
34. Rikovsky, S. Incidence of Imipramine-Induced Psychoses, *Acta Nervosa Superior* 6: 181, 1964.
35. Fotel-Anderson, K., and Gaert-Jorgensen, E.: Treatment of Endogenous Depression with Tofranil, *Ugesk-laeger* 121: 1091, 1959, (In German).
36. Klein, D. F.: Visual Hallucinations with Imipramine, *Am J Psychiat* 121: 911, 1965.
37. Blair, D.: Treatment of Severe Depression by Imipramine (Tofranil): an Investigation of 100 Cases, *J Ment Sci* 106: 891, 1960.
38. Kana, F. J., Jr., and Keeler, M. H.: Visual Hallucinations While Receiving Imipramine, *Amer J Psychiat* 121: 611, 1964.
39. Pilkington, T. L.: A Report on "Tofranil" In Mental Deficiency, *Am J Ment Defic* 66: 729, 1962.
40. Hudgens, R. W., Tanna, V. L., Harley, J. D., and Leary, D. J., Jr.: Visual Hallucinations with Iminodibenzyl Anti depressants, *J A M A* 198: 81, 1966.
41. Gradwell, G. B.: Psychotic Reactions and Phenelzine, *Brit Med J* 2: 1018, 1960.
42. Clarke, J.: Side-Effects of Phenelzine, *Brit Med J* 1: 1204, 1960.
43. Barsa, J. A., and Saunders, J. C.: Tranlycypromine in the Treatment of Chronic Schizophrenics, *Am J Psychiat* 118: 933, 1962.
44. Ayd, F. J.: Critical Appraisal of Chlordiazepoxide, *J Neuropsychiat* 3: 177, 1962.
45. Dickel, H. A., and Dixon, H. H.: Inherent Dangers in the Use of Tranquilizing Drugs in Anxiety States, *J A M A* 163: 422, 1957.
46. Klein, F., and Fink, M.: Psychiatric Reaction Pattern to Imipramine, *Am J Psychiat* 119: 432, 1962
47. Greenbury, R.: Dream Interruption Insomnia, *J Nerv Ment Dis* 44: 18, 1967.
48. Viscott, D. S.: Chlordiazepoxide and Hallucinations, *Arch Gen Psychiat* 19: 369-376, 1968.
49. Stanfield, C. E.: Clinical Evaluation of Diazepam in Psychiatric Disorders, *Southwestern Med* 44: 134, 1963.
50. Shader, R. I., Cohler, J., Elashoff, R., and Grinspoon, L.: Phenobarbital and Atropine in Combination an Active Control Substance for Phenothiazine Research, *J Psychiat Res* 2: 169, 1964.

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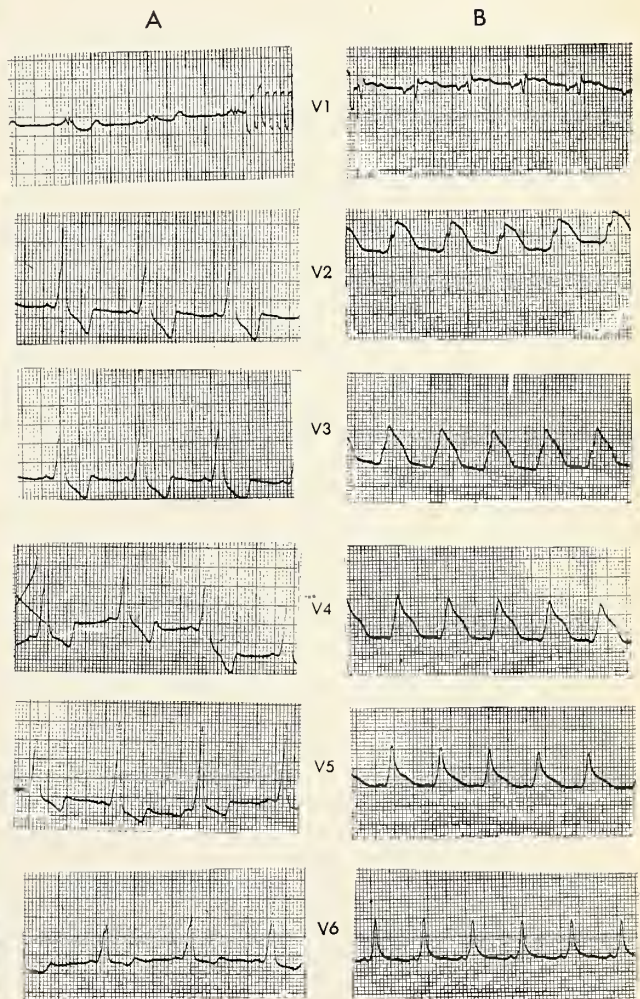
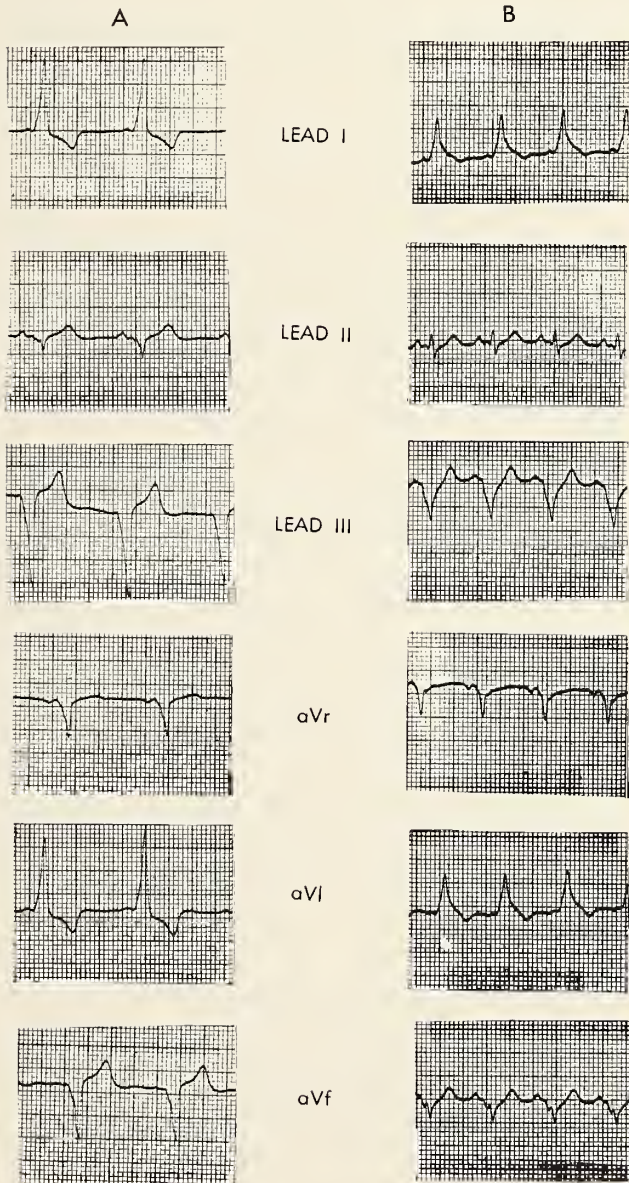
Electrocardiograms of the Month

Middlesex Memorial Hospital
Middletown, Connecticut

Submitted by:
HERBERT LEVINE, M.D.
195 So. Main Street
Middletown, Conn. 06457

W. D., 41 year old male. Tracing A was taken Sept. 22, 1967, when he was hospitalized for non-cardiac problems, and shows the characteristic configuration of Wolff-Parkinson-White syndrome.

Tracing B was taken on Oct. 26, 1968, when he was admitted to the hospital with severe substernal pain of two days' duration. Note the marked ST elevation in the precordial leads, indicative of a current of injury. Subsequent tracings over the next several days showed a similar pattern. The patient expired on the 8th hospital day, and autopsy showed extensive infarction involving almost the entire left ventricle.



WOMAN'S AUXILIARY

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HISTORY OF THE FIRST TWENTY FIVE YEARS

There is to be a Silver Anniversary celebration at the New Haven Lawn Club on Tuesday, May 6th. We hope all present and former members who are still with us will try to join us on this occasion.

At its annual meeting in May 1943, the House of Delegates to the Connecticut State Medical Society voted that the Council appoint a committee of seven members with Dr. Ralph Gilman as chairman, to inquire into the desirability of organizing a Woman's Auxiliary. Other members of the committee included Doctors Alfred Labensky, John D. Booth, Martha Clifford, Jessie W. Fisher, Cole Gibson, and E. Myles Standish.

In the Fall of 1943 the committee recommended to the House of Delegates that a Woman's Auxiliary be established in Connecticut, and that an Advisory Committee be appointed annually beginning with the 1944 annual meeting of the House. The By-laws of the National Auxiliary provide that State Auxiliaries can be organized only with the permission of the State Medical Societies and that all of its important projects must have the approval of the Advisory Committee of its own State Medical Society. Thus a liaison between the State Auxiliary and its Medical Society is firmly established.

A meeting of the wives of members of the Connecticut State Medical Society was arranged to take place at the annual session of the State Medical Society in May 1944. Mrs. James R. Miller of Hartford County was appointed temporary chairman of this organization meeting. The officers elected to represent the newly-formed Woman's

Auxiliary to the Connecticut State Medical Society were:

President, Mrs. Bertram Lambert, Fairfield County
Vice-President, Mrs. Creighton Barker, New Haven County

Secretary, Mrs. Charles Goff, Hartford County
Treasurer, Mrs. Julian Ely, New London County

Mrs. Eben Carey, National President of the Woman's Auxiliary to the A.M.A., outlined the aims and objectives of the Auxiliary. At that time there were forty organized state Auxiliaries. Connecticut was the forty-first. The principal areas covered were: Health Education, Public Relations, Legislation, Philanthropy, promotion of subscriptions to "Hygeia" (*Today's Health*), and the promotion of some social activity within the profession. In keeping with changes made by the National Auxiliary of which we are a component part, our State Auxiliary has made changes and generally enlarged its activities through State and County committees.

Health Education activities have brought about membership in and Board Representation on the Connecticut Nutrition Council, the Connecticut Advisory School Health Council, which has been the prime factor in modernizing health education in the public schools, the Connecticut Health League, and the Connecticut Health Careers Council.

Public Relations has become *Community Service*. Activities of this committee included a survey of "Existing Health Agencies" in 1949, sponsorship of a State Child Health Conference, manning of health booths for the Medical Society at County Fairs, (In 1966 the Auxiliary made and displayed a Safety project in the form of "Nightmare House" showing the many safety hazards in a home), hours

of volunteer time at Diabetes Detection booths, Polio clinics, Well-child conferences, Immunization clinics. Pre-school Vision screening, Glaucoma Detection clinics, and attendance at Governor's conferences on Recreation, Problems of the Aging, Homemaker Service and Traffic Safety.

Nurse Recruitment was added in 1948 and changed to *Health Careers* in 1960 to include over one hundred various career opportunities in the health field. High School assemblies have been arranged with showings of a film, "Helping Hands for Julie" and panels including a physician and representatives of other health careers. Scholarships have been provided by the counties in an ever more diversified range of health-oriented professions. Health Careers Guidebooks, "Horizons Unlimited", "Today's Health" and "Today's Health Guide" have been distributed in high schools.

Legislation committees have supported the Connecticut State Medical Society in its stand on National and State Bills such as the Jenkins-Keogh Bill (1959), the Forand Bill (1960), King Anderson and Kerr-Mills Bills (1962), Animal Research and Fluoridation (State Bills). In 1962 COMPAC was formed and Auxiliary members helped in the Political Symposium sponsored in 1964. Since then the Auxiliary has been represented on the COMPAC Board of Directors. More recently the Auxiliary has been involved with the Medical Society in publicizing the pros and cons of Medicare and Eldercare.

Publications—The Quarterly originally published in mimeographed sheets is now printed four times a year and sent to every member. The National Bulletin originally sent to subscribers and serving primarily as a source of information, is now a woman's magazine concerned primarily with the life and hobbies of various physicians' families, is sent to every member and is titled "MD's Wife".

International Health—In Connecticut the work of this committee consists primarily of collecting medical books and magazines for the Darien Book Plan which sends them to under-developed countries and collecting soaps, bandages, Johnnie-coats, etc. for the same purpose.

A.M.A.-E.R.F., formerly known as AMEF, has been receiving contributions of cash for the new Research Center at A.M.A. headquarters, financial aid to Medical Schools, and to the Medical Students' Loan Fund. Money for this is raised by the counties through sale of Christmas cards, playing cards, and other items, as well as through card parties, theater parties, and direct cash contribu-

tions. In 1968 the Connecticut Auxiliary contributed \$3,000 and the combined total from the fifty states was approximately \$390,000.

Membership has grown over the years from the original sixty-seven to a maximum of 1307 in 1957. Since then the number has fluctuated and is now 992. Nationally it has grown largely through the "Joint Membership" plan whereby the physician automatically includes his wife with his medical Society membership. This is not true in Connecticut.

Thus, the Auxiliary's activities have gone on these twenty five years. There have been general membership meetings twice a year at which the atmosphere has been largely social. It has been impossible to include in this history an account of the many contributions of time that have been made by our members. These are covered in the record in the archives of the Woman's Auxiliary to the Connecticut State Medical Society.

Placement Opportunities

(Continued from page 278)

training in areas of special interest. Special arrangements can be made for residents to be accepted for degrees in community mental health and hospital administration at Yale School of Epidemiology and Public Health. Personal analysis can be easily arranged. Many fringe benefits. Send all particulars in first letter to Mehadin K. Arafah, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

EDUCATIONAL OPPORTUNITY—GENERAL PRACTITIONER to specialize in psychiatry. For psychiatric residency available in a community-oriented mental hospital associated with Yale, which provides clinical demonstrations, teaching and supervision in hospital. Opportunities for training in areas of special interest. Psychoanalytic training available at Western New England Psychoanalytic Institute. Liberal fringe benefits. Send all particulars in first letter to Mehadin K. Arafah, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

WANTED—PHYSICIAN: Extensive general practice available due to death of physician. 7-room suite in new medical building, equipment and supplies. Reasonable terms, Groton-Ledyard area.

OBITUARY

Harry S. N. Greene, M.D.

1904-1969

Dr. Harry Greene died on February 14, 1969. Since 1950 he had been Anthony N. Brady Professor and Chairman of the Department of Pathology at Yale. Dr. Greene will be long remembered not for these titles about which he cared little, but



rather for his inspiring qualities as a man and as a teacher, and for his outstanding investigations in the biology of cancer.

This native Rhode Islander, a "swamp-Yankee", as he termed himself, was unusually endowed with the keen intellect, wit, humor, and rugged independence of a New England country lad. These qualities he brought with him to Yale after thriving on the educational opportunities at Brown and at McGill, and on the scientific freedoms of the Rockefeller Institute. With such natural gifts of mind and heart and with such a fine scientific background it is not surprising that he quickly became a leader in his chosen field, the experimental pathology of cancer. He learned to grow human tumors in the anterior chambers of animals' eyes thus opening opportunities for the study of their growth and control by every conceivable technique. Increasingly, the possibilities of this biological system are being exploited by oncologists, virologists and biochemists interested in cancer. The value of Dr. Greene's observations and of his experimental system will grow for many years to come. In 1956 he received the Borden Award for these original investigations. Just as important as were his own

scientific discoveries was his role of irritant or gaddy among his investigative colleagues. Trends, fashions, complacency, pretense in science he instinctively opposed and never failed to say so. This quality, so characteristic of the man, won him many fast friends and a few equally devoted enemies. He cherished both.

Dr. Greene's colorful and salty personality, his clear-headedness in scientific matters, and his directness, simplicity, and friendly nature attracted and inspired students of all ages and made communication with them easy. He immediately became and remained their champion. We have lost in him a truly "complete" man—scientist, teacher, champion and friend. In a life-time such come only rarely.

Levin L. Waters, M.D.

In Memoriam

Gillespie, Harry—Hartford, Jefferson Medical School, 1934. Dr. Gillespie was a general practitioner in the Hartford area for over 20 years. He was associated with the Mt. Sinai, McCook, Hartford and St. Francis Hospitals. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medical Association and the American Academy of General Practice. Dr. Gillespie died January 3, at the age of 61.

Hervey, Zoltan P.—East Hartford, University of Vienna Medical School, 1938. During World War II, Dr. Hervey served as a captain in the U.S. Army. He was associated with Mt. Sinai, St. Francis, Hartford and Manchester Memorial Hospitals. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, and the American Medical Association.

Dr. Hervey died January 25, at the age of 55.

Spillane, Bernard—Bloomfield, Tufts University School of Medicine, 1916. Dr. Spillane was a urologist in the Hartford area for over 40 years. He was associated with Hartford, Mt. Sinai, McCook, and Bristol Hospitals. He was a member of the Hartford County Medical Association, the Connecticut State Medical Society, the American Medi-

cal Association and the American Urological Association. Dr. Spillane died December 15, at the age of 79.

Staub, Philip L.—Fairfield, Long Island Medical School, 1939. Dr. Staub was an orthopedic surgeon in the Fairfield area for 20 years. During World War II, he served as a major in the U.S. Army. He was associated with the Bridgeport and Park City Hospitals. He was Medical Director of the United Cerebral Palsy Association of Fairfield County and was assistant associate professor of Orthopedics at Yale University. Dr. Staub was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, the American Medical Association, and the American Academy of Orthopedic Surgeons. He also was a fellow of the American College of Surgeons. Dr. Staub died February 5, at the age of 52.

White, William M.—New Canaan, University of Michigan Medical School, 1943. Dr. White was a practicing psychiatrist in the New Canaan area for over ten years. He was a member of the Fairfield County Medical Association, the Connecticut State Medical Society, and the American Medical Association. Dr. White died January 30, at the age of 51.

Doctor's Office

Leonard A. DeFusco, M.D., announces the opening of a second office for the practice of obstetrics and gynecology at 47 Burnside Avenue, East Hartford.

Harold A. Engelke, M.D., announces the opening of an office for the practice of general medicine in the Medical Arts Building, Torrey Park, and Route 12, Ledyard.

Marie J. Fakkell, M.D., announces the opening of an office for the practice of obstetrics and gynecology at 122 Hoyt Street, Stamford.

Saul Feierstein, M.D., announces the opening of an office for the general practice of medicine at 884 Main Street, Monroe.

Charles D. Guri, M.D., announces the opening of an office for the general practice of medicine at Burlington Road, Harwinton.

John Jacob Haksteen, M.D., announces the opening of an office for the practice of psychiatry at 85 Jefferson Street, Hartford.

Patrick Mulhern, M.D., announces the removal of his office for the general practice of medicine to 94 Washington Avenue, North Haven.

Ronald C. Savin, M.D., announces the opening of an office for the practice of dermatology at 299 Seymour Avenue, Derby.

Forensic Odontology Seminar May 7, 1969—Hartford

The Connecticut State Dental Association in cooperation with the Connecticut State Police Department is conducting an all-day seminar and training program in forensic odontology on Wednesday, May 7th, 1969 in Hartford, Connecticut.

The purpose of the meeting is to create a reservoir of trained personnel, who will be available for helping the state police and federal agencies in identification problems associated with disasters such as floods, fires and aircraft accidents.

While specific emphasis will be given to the dental aspects of identification, nevertheless the program is designed to include many of the standard techniques in the field.

All interested physicians are asked to contact Dr. Lester L. Luntz at 111 Pearl Street, Hartford, Connecticut 06103, for further information and registration. There is no fee.

News From Yale University School of Medicine

Dr. George Rosen, noted medical historian and authority on public health education now on the staff of Columbia University, has been appointed to the faculty of Yale University.

He will hold a joint appointment here, as Professor of the History of Medicine in the Yale Graduate School and as Professor of Epidemiology and Public Health at the Yale School of Medicine. His appointment is effective July 1, 1969, according to a recent announcement by Charles H. Taylor, Jr., Yale Provost.

Many years of service with the New York City Department of Health and the Health Insurance Plan (HIP) of New York, in addition to his academic career, have given Dr. Rosen a wealth of experience in public health, specifically in medical care and in public health education. He has also had an extensive career as a scholar and editor in the field of the social history of medicine.

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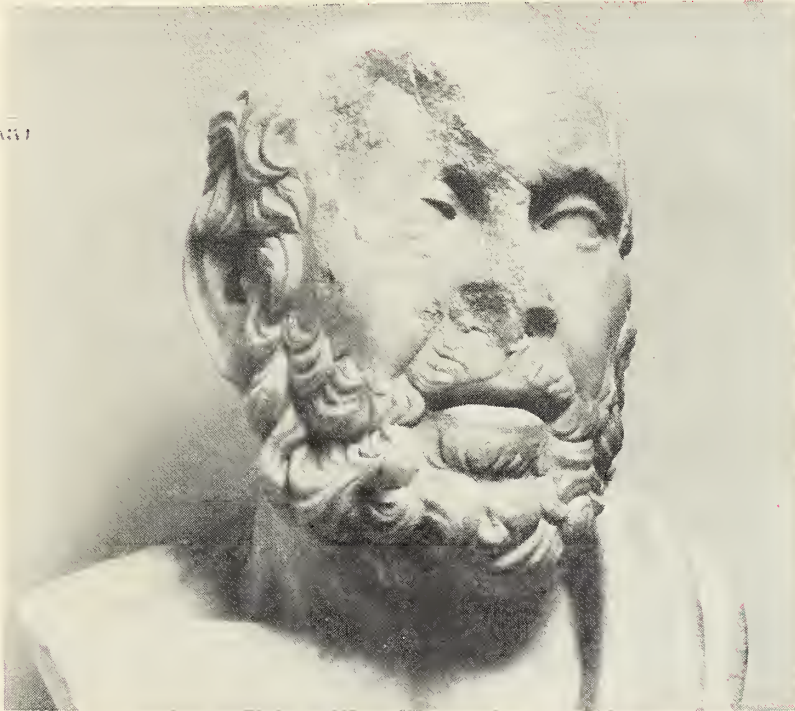
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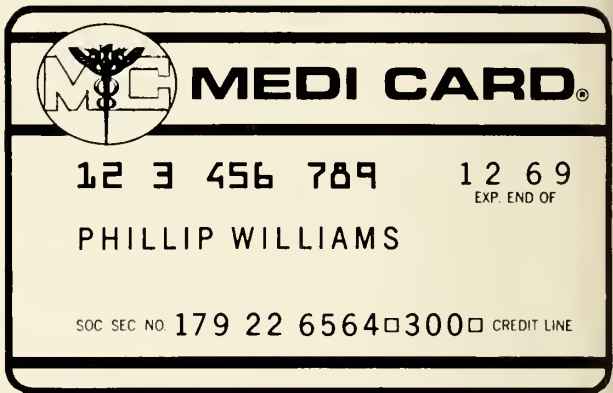
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Connecticut Medicine

editorials

Hippocrates Of Ostia

The Law: Whoever intends to acquire truly an understanding of medicine must be possessed of these things: natural ability, instruction from childhood, good teaching, a favorable location, diligence, time.—Hippocrates.

Dickinson Richards¹ has given us a learned and authentic picture of Hippocrates accurate and vivid. How was it possible to reach back into the shadows 2400 years ago, find the man, distinguish and identify him out of the myths, legends and errors that obscure him? Read his account. The great hero was born on the Island of Cos near the Asian mainland about 460 B.C. and died and was buried near Larissa in Thessaly around 370 or 360 B.C. Thus his life spanned approximately those of Socrates and Plato combined and he died when Aristotle was a young man.

Hippocrates received his training in medicine from Heraclides. He studied Philosophy with the great Democritus whose ideas of space, of individual particles occupying space, their rearrangement and movement, and especially the mechanistic explanation of nature excluding both soul and di-

vine powers, were centuries ahead of their time. In this tradition Hippocrates insisted on direct observation of natural processes as the whole explanation of the events of health and disease. The Greek physicians of whom Hippocrates was the greatest, were the first to take data about patients and transform it into knowledge. Thus where their forerunners had noted details, moments of sickness as it were, the Greeks encompassed the whole body of illness. "The Greeks invented the science of medicine." This is beautifully stated by Hippocrates in Epidemics: "State the past, diagnose the present, foretell the future (history, physical examination, and prognosis)."

Much fable has grown up about him. He is said to have travelled widely, restored health to King Perdicca of Macedonia, cured the "insanity" of his friend Democritus, and helped the distant Illyrians stay the plague although Thucydides states that all efforts were in vain. He received many honors. Aristotle in the generation after Hippocrates called him the Great Hippocrates and commented on one of the writings of the Hippocratic School—The Nature of Man. The Hippocratic writings, the so-called Hippocratic Corpus,

ABOUT THE COVER

In the excavation of the ruins of Ostia Antica, the seaport of imperial Rome, there was uncovered in the year 1940, the family tomb of a distinguished Greco-Roman physician, K. Markios Demetrios, who died about 100 A.D. On the ground in front of the tomb was found a head, in marble, of an elderly bearded man, and near this, a pedestal with an inscription beginning, "Life is short". On further study, it was discovered that this head corresponds closely, in general conformation, face, beard, and other detail, with that on a Roman coin of the Island of Cos, of the first century A.D., which also has on it the letters "Hip", and the emblem of serpent and staff; long recognized as a representation of Hippocrates. This new sculptured head is thus also identified as that of Hippocrates. From this and other evidence, archeologists and historians are now in fairly general agreement that "Hippocrates of Ostia" does indeed represent what antiquity accepted as his likeness. In spite of the fragments broken off from the right side of the face and nose, it is seen to be a head and countenance of great power, with an expression combining in a remarkable way both sensitiveness and strength.

The sculpture itself is of Parian marble, a fine Roman copy of an earlier Greek original. It is clearly Hellenistic in style, and from this the original can be dated as having been made about 300 B.C.—Dickinson W. Richards, M.D.

contains some 70 treatises of varying length and character and probably there were also many others that were lost.

Richards points out that there are seven treatises which are recognized by authorities as having been written by one man presumably Hippocrates himself. In them we find accuracy of observation, precision of his descriptions of disease and freedom from philosophic theory. Even when he offers explanations of disease processes, the bodily "humors" and "forces" the clinical "crises," "coction" of malignant acid discharges into blander, thicker ones, the "blending" of all actions, in the state of health—all these were concerned not at all with general philosophic ideas, but solely with an evaluation of the disease process or the patient, or his treatment, or his prognosis. From all this one suspects that Hippocrates was an even more remarkable physician in action than he himself put into words.

As far as the Oath is concerned, Edelstein² believes that the philosophical background of the Oath is clearly Pythagorean and post-Hippocratic. He credits the general acceptance of the Oath in recent centuries to the coincidence that many of the Pythagorean concepts were shared by Judeo-Christian ethical writers. Nevertheless even if the wording is not Hippocratic, the ethical content is largely consistent with the genuine Hippocratic writings. In recent years since the Hitlerite practice of genocide the "Oath" has been replaced by the Oath of Geneva in which the physician dedicates himself to work in the best interest of the patient and to work in the interest of humanity.³

Inevitably we want to know what our hero said, how he acted and perhaps especially what he looked like. Soranus describes Hippocrates the man as bald, grave in manner, neglectful of money, and as teaching the art to his students "frankly and liberally." Historians have proposed various ancient coins, medallions and sculptures on the true likeness of Hippocrates. But none of these art works has been completely convincing and scholars have continued to search for a more authentic example of portraiture. Richards describes a bust in a scholarly presentation found in 1940 near Ostia Antica, Italy.

On one of the pedestals was an inscription beginning "Life is short." The remainder did not complete the first Aphorism but was an appropriate funerary sentiment as follows: "Short is life but long the aeons that we mortals spend beneath the earth. To all is given part in the divine fate whatever it be." On the ground beside this pedestal

was found the bust of an elderly bearded man (see front cover) with fragments of the nose and right side of the face unfortunately broken off.

The bust was found to fit on the pedestal but the latter had been adapted to the bust as though the bust might previously have been placed elsewhere. Professor Giovanni Becatti now Professor of Archaeology found that this head corresponds closely in important detail and general configuration with the Hippocrates on Roman coins of Cos. Four other busts have been identified of the same individual with all the details of face, eyes, facial lines, beard etc. as this one but none of them with the same skill in sculptured modelling. The identification of this head with Hippocrates is thus about as secure as archeological evidence is likely to be. Though much damaged it is a sensitive and interesting face totally different from all others previously thought to be Hippocratic.

Where did it come from. It is a fine Roman copy in Greek marble of an earlier Greek original. Miss Richter dates this original Greek sculpture, by its style, demonstrating as it does "full blown realism" of the Hellenistic age, as belonging to the latter part of the third century B.C. We now have a marble bust which is in Richard's laboratory made from a plaster cast of the statue at Ostia Antica.

L.H.N.

References

1. Richards, D. W.: Hippocrates of Ostia. *JAMA*, 204: 1049, June 17, 1968.
2. Edelstein, L.: The distinctive hellenism of Greek medicine. *Bull. Hist. Med.*, 40: 197, 1966.
3. Nahum, L. H.: A definition of death: Ethical and legal questions posed by recent advances in medicine. *Conn. Med.*, 32: 779, November 1968.

Origin Of Cancer: II. Contact Inhibition Of Growth In Cell Culture

The close relationship between cell movement and mitosis is strikingly evident in the case of many normal cells which form monolayers in suitable substrates in-vitro. There is a dramatic fall in mitotic rate sometime after the monolayer has become fully confluent and the individual cell movement has effectively ceased. This phenomenon has come to be called "contact inhibition of growth, not however to be confused with the contact inhibition which is concerned with cell movement.

The formation of a monolayer on a particular substrate implies obviously that the relative adhesion between cell and substrate is greater than be-

tween cell and cell. In these conditions the cells will spread and multiply until the available area of substrate is occupied. If the cell should have identical surface properties this would then result in an equilibrium position in which each cell has an equal share of the available surface. It is at this point that cell movement ceases and the membrane of each cell becomes stabilized. The onset of DNA synthesis means onset of mitotic control. The cessation of mitosis will therefore follow the establishment of a thermodynamically stable arrangement of cells but not before this occurs. It is probably also true that mitosis itself may tend to interfere with progress towards an equilibrium, because in several reported instances several layers of cells may be built up before the equilibrium is achieved.

When a single cell is placed on a substrate such as glass it seems to remain chronically unstable. Its outline can be continually changing and the cell margin may show continuous ruffling movement. Carter has interpreted this ruffle formation on the same principles of competitive adhesion as those which seem to control the movement of the cell as a whole. In this view a ruffle represents a local displacement of the cell by culture medium from an area of substrate which has been contaminated by cell contact. It is probably significant that ruffling of the cell margin is often associated with pinoctosis, a condition in which the cell membrane is free to change and invaginate. In a confluent monolayer ruffling is no longer a prominent feature of the cell margin and its absence appears to reflect the physical stability of the cell population as a whole.

This manner of study of "contact inhibition of growth" may prove to be the simplest and most valid approach to understanding the basis of mitotic control. The extensive semantics which has grown up around this subject tends to assume that the effect is mediated by the transfer of specific chemical substances. Thus such expressions as that cells can "recognize" "signal" or "communicate" with each other are in a sense meaningless without at the same time describing how they achieve this result. These words may be highly misleading in fact, because they do not fit at all well with those explanations which are primarily concerned with the physical properties of surfaces.

The mechanism that Carter proposes for contact inhibition of growth suggests that it should be dependent on the surface properties of the substrate. If this were so then it would be very difficult

to reconcile it with an explanation based on the concept of chemical signals which can be exchanged between one cell and another.

L.H.N.

Reference

1. Carter, S. B.: Tissue homeostasis and the biological basis of cancer. *Nature*, 220: 970, December 7, 1968.


Origin Of Cancer: III. Nature Of Malignancy

One feature of malignancy which receives little or no attention in current theories of cancer is the variation which exists between the cells of the same tumor. The pathologist has long recognized it by the differences in the size and shape of the individual cells, their nuclear morphology and staining characteristics. In tissue culture transformed into malignant clones there is enhanced variability in electrophoretic mobility. And, of course, the cytologist has long recognized a variation in chromosome number. Such widespread and universal features of cancer must clearly be taken into account in any satisfactory explanation of malignancy. These variations could be the result of a breakdown of the control mechanisms or they might be not the result but the cause.

In a population of malignant cells, if the surface properties are randomly different and if each cell is moved accordingly to the surface forces acting on it, then it is apparent that such a population is unstable. Assuming no new cells were added to the population, the cells would ultimately achieve a thermodynamically stable arrangement although the clone would never show a normal tissue architecture. However, the instability of the population induces further cell division and the emerging pattern has to be continually changed to accommodate these new cells. In this way the instability of the cell population becomes self-perpetuating and growth control is lost.

In normal cell division there is equal distribution of genetic material between the two daughter cells. If chromosomal DNA is not accurately copied, separated and distributed, this could result in unequal distribution of genes, resulting in daughter cells which are not precisely the same. Cells which have been treated with carcinogenic chemicals, or exposed to X-ray, often show abnormalities of the mitotic mechanism. This may be especially apparent in the anaphase. Damaged chromatids may fail to separate cleanly and the genetic material is torn apart and distributed unequally between the daughter cells. Should the damage now persist,





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it will interfere with subsequent copying or separation, the unequal distribution of genes will remain so that the entire clone will show an abnormal degree of variation. Oncogenic viruses produce essentially similar effects.

In this view genetic damage need not be specific in any chromosome or gene to produce malignancy. It needs but to produce variation in the cell surfaces. Another feature of cancer is that tumors derived from the same cell type can vary greatly in malignancy. A continuous range would be possible according to the degree of variation in the cell surface that result from the originally damaged chromosome or chromosomes.

One fact that demands an explanation is latency in appearance of tumor between exposure to a carcinogenic hazard and the clinical onset of cancer. Carter's view is that once variability in cell surface has been achieved, a clone develops. As long as it is small, minor adjustments between its component cells could restore local thermodynamic equilibria and general stability. If and when the clone reaches a critical size depending on the degree of surface variation involved, the instability becomes self-perpetuating and homeostatic control is permanently lost. It is likely that most potential tumors never reach this critical point. Similarly one metastatic cell is unlikely to develop into a secondary tumor, but a clump of detached tumor cells which already exceed the critical size will develop immediately into a metastatic growth. Such an idea if true could have important implications for the therapeutic control of metastatic spread.

What now happens to the normal cell at the edge of the tumor. One event could be normal and malignant cells intermingling. If incorporated into a tumor, a normal cell could develop increased mitotic rates and contribute to overall variability. This would immediately release its malignant potential. It would act by promoting malignancy in a hitherto normal cell. This concept of "promotion of malignancy" can be extended to any factor which causes a local increase in mitotic rate. Thus hormones may have a promoting action in some situations and chronic physical irritation could be regarded in the same category. Carcinogenesis by implanted plastic films could also result in promotion. By creating an "unhealable wound" they may bring to light any potentially malignant cell in the region.

Cells in non-confluent culture are usually highly

unstable and show a high rate of mitosis and spontaneous transformation is common. It is highly significant that when cells are deliberately transformed in culture by viruses or chemicals, they do not show a latent period. Apparently cells which are appropriately damaged in-vitro are not subject to the restraints which would be imposed in-vivo and therefore no critical clone size has to be achieved before these restraints are overcome. Cells transformed in this way pile up on certain substrates. They have lost their "contact inhibition of movement." Can it be that they have a stronger relative adhesion to each other than to the substrate.

There have been experiments designed to investigate the phenomenon of contact inhibition of growth such as those in which two normal cell lines which independently demonstrated contact inhibition of growth, failed to do so when mixed together. When mixed it enhanced the variability of the cell population as a whole and this hindered the formation of a stable arrangement.²

The concept that malignancy is due to variability in cell surfaces ought now be subjected to experimental verification. The most direct testing of the idea would be to create a physical environment with which a single isolated cell would establish a stable adhesive relationship. Such a cell should show an inhibition of mitosis which is independent of its normal or malignant origin. Attempts to create such an environment in the single cell scale have so far proved unsuccessful. Stabilization of the cell membrane is theoretically attainable simply by suspending the cell in a fluid medium.

Present standard methods of suspension culture subject the cells to repeated collision with other cells and the vessel walls. If potentially unstabilizing factors such as these were eliminated, then suppression of mitosis would be anticipated for all suspended cells irrespective of their malignant or normal nature. Conversely a physical environment designed to create instability in the cell membrane would be expected to promote the growth of culture cells. Carter¹ has made some preliminary experiments of this type which have given some positive indications.

If cancer is due to random cell variation resulting from nonspecific genetic damage and does not involve any characteristic change which could lead to a potentially exploitable difference between normal and malignant cells, then the ultimate

prospect for cancer chemotherapy becomes very much less favorable.

L.H.N.

References

1. Carter, S. B.: Tissue homeostasis and the biological bases of cancer. *Nature*, 220: 970, Dec. 7, 1968.
2. Eagle, H. and Levine, E. M.: *Nature*, 213: 1102, 1967.

Studies In Cancer: IV. The Control Of Mitotic Activity By Chalone

Normal epidermal cells maintain a perfect balance between cell production and cell loss. How is this perfect balance maintained. One view is that as the cells are shed, the growing epidermal cells resume mitotic activity because of a change in their surface configuration.¹ Another view recently proposed is derived from the fact that normal epidermal cells produce a tissue-specific substance chalone or colyone which inhibits epidermal mitosis. These two views are not contradictory if we assume that chalone regulates the surface thermodynamics which in turn inhibits mitosis.²

Bullough and Lawrence³ have examined the hypothesis that the amount of chalones may be inadequately produced by tissues which have under-

gone malignant degeneration. If so this would account for uninhibited mitotic activity. They found that the cells of epidermal tumors in experimental animals contained at least some epidermal chalone. However, smaller amounts of chalone existed in the tumor tissue than was present in normal tissue. Accordingly they derived chalone from tumor tissue and treated normal epidermal tissue with it. This chalone, however, did not inhibit mitotic activity by itself although in the presence of adrenalin and hydrocortisone it did in fact control mitotic activity in normal epidermal tissue. Other experiments in-vivo, however, did show that experimental tumors in rabbits responded with marked mitotic depression to the injection of additional epidermal chalone derived from normal tissue. This observation would indicate that either tumor chalone was in insufficient supply to prevent mitotic activity or else was a degraded and inactive form of the normal epidermal chalone.

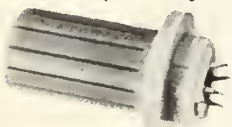
In order to determine whether chalone application has practical value in cancer chemotherapy Rytömaa and Kiviniemi investigated the control of cell production in the rat with experimentally induced leukemia after administration of granulocytic chalone. They report a series of experiments⁴ which showed that leukemic cells were capable of responding to added chalone. However, they responded with considerably less intensity in inhibition of DNA synthesis than did normal cells.

A further study in practicality and usefulness of chalone in chemotherapy of cancer was carried out by Bullough and Lawrence.⁵ They investigated mitotic control of melanomata both by epidermal and also by melanocyte chalone. The experiment showed the specificity of the chalones. There was no mitotic inhibition in the amelanocytic melanoma cells when skin chalone was used unless adrenalin and hydrocortisone were added to it. However, when chalone from melanocytes i.e. tissue-specific chalone was used, the tumor cells responded with 50 per cent mitotic depression.

It was inevitable that these experiments in-vitro should be extended to in-vivo studies on tumor inhibiting actions of chalones. Mohr et al⁶ performed experiments on mice in which melanomas were transplanted and also on Syrian hamsters in which amelanotic melanomas were experimentally produced. When the melanomas had grown to 2 cm. in diameter additional chalone was injected subcutaneously on the side of the body opposite the tumor. Cell tumors responded. They became soft and necrotic. The amelanotic melanoma darkened,

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then regressed and ulcerated and the wound finally healed.

These experiments represent the first application of the chalone concept to the control of tumor growth and tumor destruction. We now need to know whether other tumors will respond similarly to the chalone of their original tissue. What is especially important is the urgent need to know more about the nature of the chalones and on the chalone content of the various tissues. It is, however, obvious that the reported basic science investigations have opened a new and promising avenue to understanding the control of carcinogenesis.

L.H.N.

References

1. Nahum, L. H.: *Viruses And Cancer*, Conn. Med., 25: 287, May 1961.
2. Chalones and cancer. *JAMA*, 206: 2735, Dec. 16, 1968.
3. Bullough, W. S. and Lawrence, E. B.: Chalones and cancer. *Nature*, 220: 134, Oct. 12, 1968.
4. Rytömaa, T. and Kiviniemi, M.: Control of cell production in rat chloroleukemia by means of the granulocytic chalone. *Nature*, 220: 136, Oct. 12, 1968.
5. Bullough, W. S. and Lawrence, E. B.: Melanocyte chalone and mitotic control in melanomata. *Nature*, 220: 137, Oct. 12, 1968.
6. Mohr, V. et al: Melanoma regression induced by "Chalone": A new tumor inhibiting principle acting in vivo. *Nature*: 220: 138, Oct. 12, 1968.

Medical Dogma: Early Detection Of Cancer

There is a time honored concept that early diagnosis of cancer equals early growth and therefore that earlier treatment will improve the chances of survival. This concept assumes that growth behaves in an ordered way and progresses from one stage to another. This assumption is highly improbable since cytologically, cancer growth is essentially disorder and will follow the laws of disorder. Because of our natural sense perhaps it is an esthetic sense of orderliness, this has provided the conceptual basis of our treatment of malignancy from time immemorial. Brooke¹ recalls the guilt placed upon him, when a student, by the accusations of venerable seniors when a patient was referred to the hospital "too late." It was many many years later that he began to be aware that longer survival after surgery was found, not in those diagnosed early, but in those whose symptoms had persisted untreated for a longer time before operation. It was then that he became aware that "early" diagnosis gives no indication of when the lesion started nor its tendency to dissemination.

Actually there appears to be no such thing as an early case. For example a woman presents with a small swelling in the breast unattached to the skin or muscle and with no involved nodes. She knows it has not been palpable for more than a month. It is removed and found to be anaplastic, disseminative, and she is dead within a year. The diagnosis was early but was she an "early" case? By contrast there are the many cases that are "late" even with spread to the axilla where the patient lives on for years.

Recently an extensive difficult and laudable research investigation was undertaken in a London borough to "screen" women over the age twenty-five. The assumption was that "early" diagnosis would reduce the toll from cancer. Sixteen swellings were found in 654 women of whom five proved to be cancer and four were in stage I. Here on the face of it was success. But what actually is stage I. If all four cases were anaplastic then the "earlier" diagnosis will probably have been of no consequence to the outcome. Clearly we need to look at staging more closely. Staging defines the situation of spread in clinical terms when the patient is first seen. It does not indicate malignant potential.

It is dissemination that kills not local spread. Jarrell and also Bond^{2 3} pointed out that dissemination remains quiescent and the disease dormant even for many years, so that the disease progresses inexorably despite surgical interference. Surgeons do not apply the term early case or early diagnosis to cancer of the pancreas or liver precisely because we know the awful truth that with the exception of the ampullary area, the extirpation carried out at these sites are univervsally useless. Nevertheless we persist in the use of this term at sites where the outcome is less immediately obvious. Perhaps we have retained a degree of optimism and naivete about breast cancer since the 19th century by accepting "early" diagnosis as a medical dogma.

An early case simply implies that the disease has been detected at an early symptomatic stage. This does not equate with early in pathological terms. In pathological terms what we are really referring to is dissemination. Some growths are "late" the moment they start whether they can be demonstrated to have spread or not, just because their biological potential, their inmate vitality is so great. So there is no "early" stage clinically, only disseminative or less disseminative and this often remains a secret until after the specimen is obtained and the treatment which surely should be

based on this aspect has been decided upon and given.

The breast Brooke points out, is not the only example of this equivocation. The colon and rectum has come under recent review in Birmingham where 12,494 cases were seen between 1950-61 in that region.³ The crude five year survival rate remained around 21 per cent throughout the period and was no better than it was in the same region for the years 1936-51. Yet over this period of time medical services had improved in availability application and technique. More patients must be receiving treatment earlier in the clinical course. Here again the best survivors were found among those with the longest history.

Brooke holds that if the concept of early recognition of disease does not improve mortality figures then the concept of the "early" case must be wrong. The figures cannot be "improved" because they reflect not our ability to catch the disease at an early stage of ordered progression but simply the type of disease as is ordained at its onset. Stated another way: 15 per cent of all cases with rectal cancer are fortunate enough to have a growth with a low dissemination potential, and this has no relationship to the time at which the patients are first seen. Is this reality or pessimism?

We do not have to conclude that excision of a growth makes no difference in survival or even cure. Surgery certainly has an unassailable place in palliation. The more sluggish the growth the better chance there is of its being caught before it has escaped its bounds and it is in this group that surgeons should apply their expert techniques. The only point is that we must not delude ourselves into thinking that this will make any substantial difference in survival statistics. As far back as 1951 Park and Lees found no evidence that surgical treatment affected the five year survival statistics in breast cancer although it was possible that conventional methods might have increased survival by 5-10 per cent. McKinnon however was more gloomy.⁴

There must therefore be a small fringe in whom we can encompass the lesion in terms of local spread, of invasion in fact, in whom dissemination has not occurred. The real question then is how do we recognize this group. This is not easy in breast or large bowel without the specimen to examine and as yet no means have been found to correlate dissemination potential with histological appearance of the primary lesion. What we must search for in the next decade is a technique where-

by cytology may either foretell the growth or its potential when it has occurred so that we may treat each case appropriately. The statistics will only be improved by "predictive cytology", predictive in more than the diagnostic sense but predictive of dissemination.

What Brooke emphasizes is that the concept of the early stage is dogma, a particular connotation without meaning. It could have meaning when we learn to recognize the cancer which is yet confined. At present we cannot know this since clinical evidence can give us no assurance as to where the cells have strayed.

By retaining the concept of the early case we divert attention from the real need of today, the need to discover means of detecting dissemination not just local spread, by clinical investigation or at second best by detecting indications of dissemination from biopsy material.

L.H.N.

References

1. Brooke, B. N.: Early detection of cancer. *Lancet* II, 1289, Dec. 14, 1968.
2. Jarrell, A. S.: Editor in *Syntax Symposium on Treatment of Carcinoma of the Breast*. p. 3, London, 1967.
3. Bond, W. H.: *Ibid*, p. 24. London, 1963.
4. Slaney, G., Waterhouse, J. A. and Powell, J.: Paper presented to the British Society of Gastroenterology on November 8, 1968.

Starvation Of The Infant And Brain Size

Undernutrition in laboratory animals has been shown to result in permanent impairment of brain and body growth, in decreased brain cholesterol in decreased synthesis of cerebroside sulphate and in decreased brain cellularity. The number of cells in the brain was determined by measuring the amount of DNA present. This is based on the assumption that DNA is constant in each nucleus. All such studies involved analyzing the whole brain for DNA content and this of course could not measure possible alterations in DNA in the various individual parts of the brain. Now Chase et al¹ have published data on the effect of malnutrition in the cerebellum as well as the cerebrum.

The infant rats were undernourished by forcing young mothers to nurse 16 instead of the 4 infants. They were then killed at 18 days. The brain and brain stem dissected free of meninges and then divided into cerebrum and cerebellum. The total brain weights were much lower in undernourished than well nourished animals with the difference in

body weights being considerably greater than the difference in brain weights. The weights of both cerebrum and cerebellum fractions were considerably lower in the undernourished animals with cerebrum averaging 9.9 per cent lower and cerebellum 18 per cent lower than the controls.

The DNA content of the brain as determined by a satisfactory method was significantly lower in the undernourished animals but remarkably the reduction was almost entirely in the cerebellum and barely in the cerebrum. Why the cerebrum grew normally but the cerebellum lagged significantly in growth in the undernourished animals is an important subject for further study. The method of course is valid in judging the number of brain cells only if there is a constant amount of DNA in each cell of the tissue being examined. Therefore it is valid for the cells in the cerebral fraction. However, polyploidy is well known in the cerebellum and therefore it is still uncertain whether the lower content of the cerebellar DNA represents fewer cells or only a reduction in polyploidy.

From previous studies it was discovered that the total protein content of the brain of undernourished animals is also less than in normal brains. Chase's study confirmed this finding and went further to show that the percentage difference is much greater in the cerebellum, 28 per cent, than in the cerebrum (only 4.6 per cent). Brain cells in undernourished animals contain more water than those of well nourished animals of the same age. Thus the effect of undernutrition can be interpreted as less protein and smaller cells in the cerebrum. The cerebellum seems to be more severely affected by undernutrition than the cerebrum with considerable effects on weight, DNA and protein all suggesting that cell number but not cell size is influenced.

The timing of the undernutrition may be important in determining whether the observed effects are permanent as well as which tissue is effected the most. In the first 9 days there is found less DNA in cerebellum but not in the cortex undernourished animals. Then at 9 days they were well nourished and when killed at 21 days the cerebellar deficit had disappeared. It should be noted that in the rat the period of rapid brain growth begins 6 days after birth diminishing to 23 days after birth. Approximately 10 per cent of rat brain DNA is present at birth with synthesis stopping after 17 days.

This is in contrast to the period of rapid brain growth in the human which commences in utero,

reaches a peak near birth and continues in the first year after birth. It appears that the production of brain DNA is two-thirds complete by birth and ceases 5 months after birth. What we need to know is whether and to what extent malnutrition in the human has the same deleterious effects as post-natal malnutrition in the rat. Chase recently examined two children who suffered from severe malnutrition in the first 8 months of life and who showed evidence of cerebellar damage at age 4-5.

There have been clinical and epidemiologic studies which suggested that in the human there is a critical period in the maturation of the nervous system at which time adverse influences have a profound and permanent effect. They exhibit a delayed psychomotor development particularly if the deficiency has been early in infancy and despite an adequate diet thereafter. Biochemical correlates of such clinical observations have yet to be established and will require the study of many cases with adequate social and individual histories.

Fishman² has now presented evidence on the lipid composition of the human brain in chronically malnourished infants. The results demonstrate that the changes in brain lipids of starving infants resemble those reported for experimental animals. In particular there is a reduction in total lipid content and those classes of lipids of which myelin is composed are most severely affected. There are admittedly some difficulties in human studies. Adequate clinical histories are difficult to obtain. When they are available mothers are often found to have been malnourished during pregnancy and the infants to have been born of relatively low birth weight. Thus the effects of intra-uterine malnutrition cannot be separated from malnutrition suffered during infancy. There may also be terminal aberrations in water and electrolyte content.

Whether the synthesis of the myelin membrane of the neuron which is most affected by undernutrition in humans as well as in animals is primary or secondary is not clear from Fishman's study. The failure to produce myelin could be secondary to a failure to elaborate neural elements or to increase of oligodendrocytes. Histological studies show that undernutrition impairs the elaboration of neural processes, and as we have seen above, biochemical studies indicate that the content of DNA is reduced in those conditions.

It would seem axiomatic that no tissue can grow without adequate nutrilites to sustain growth. During critical periods of brain growth proteins and



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calories in sufficient amounts are necessary to increase number of brain cells and all their elements including DNA, protein and myelin. The work of Chase¹ and Fishman² are documenting this biological principle for the growth and function of the nervous system. There must also certainly be close correlates between number of cells and intellectual function.

L.H.N.

References

1. Chase, H. P., Lindsley, W. F. B. and O'Brien, D.: Under-nutrition and cerebellar development. *Nature*, 221: 554, Feb. 8, 1969.
2. Fishman, M. A., Prenskey, A. L. and Doge, P. R.: Low content of cerebral lipids in infants suffering from malnutrition. *Nature*, 221: 552, Feb. 8, 1969.

Nutrition And Intellectual Achievement

Recent data have indicated that some of the conditioning factors that lead to behavioral characteristics of the older child are not psychosocial in nature but actually have a biochemical basis. If one alters the biological and physical environment one can produce profound and lasting disturbances of the anatomical chemical and thus developmental and behavioral pattern of the organism. The best studied aspect of biochemical conditioning of the organism is that of nutrition. In most areas of the world malnutrition in early life is directly or indirectly responsible for more deaths among children than all other causes combined. Recent evidence has indicated that deficiencies in nutrition not only affects physical growth but can produce irreversible mental and emotional changes.

As far as physical growth is concerned we know that malnutrition retards physical growth in animals. If growth is suppressed for a sufficiently long period during a critical phase in the early weeks or days of life subsequently supplementation of the diet while initially enhancing the rate of growth, usually does not permit the animal to obtain its normal mature size. The same sequence of events has also been demonstrated to occur in children who had suffered from severe malnutrition during early life. Maturation of a variety of biochemical processes is delayed and this may under certain conditions produce retrogression to earlier functional patterns.

In malnourished children water distribution, fat absorption, concentration of plasma lipids and cholesterol and excretion of creatinine approximate corresponding values observed in well nourished younger children of the same height and weight.

Metabolism of phenylalanine to tyrosine is depressed in malnourished children. This suggests that the enzyme system responsible for the conversion of the one amino acid has either been depressed or not fully developed, a finding which is normal in much younger infants. In older children malnutrition affects the ability to metabolize aromatic amino acids and tend to resemble those associated with inborn errors of metabolism. This raises the urgent question as to how such defects affect the development of the central nervous system (CNS).

There are two separate phases in the development of the CNS. One of these, maturation, consists of a rapid increase in cells as indicated by the increased concentrations of DNA phosphorus. The other phase parallels myelination and is represented by an increase in cholesterol. In the pig, rate of maturation of the CNS peaks prior to birth whereas the rate of growth of the CNS peaks shortly after birth. If inadequate nutrition in calories and proteins coincide with the period in life in which the brain is growing most rapidly, the result will be a brain which is smaller at maturity and one which also matures at a slower rate biochemically and functionally. Such a result occurs in a rat which is underfed for only a few weeks after weaning even if it is placed on an adequate diet after this. Myelin synthesis is decreased at a time when myelination should be most active that is in the vulnerable period for the developing CNS.

The brain of the mature rat malnourished during infancy is physically smaller but also shows degenerative changes of neurons and neuroglia cells. In the adult rat however starvation does not result in changes in brain weight or similar damage to neural tissue. In the human infant inadequate feeding of pyridoxal phosphate which serves as a coenzyme for most enzymatic reactions of amino acids, results in a series of changes in the physiological function of the brain and in the appearance of clinical symptoms. A newborn baby ingesting a diet deficient in this vitamin but otherwise adequate, results in six weeks in hyper-irritability, convulsive seizures, abnormalities in development and behavioral disorders. Should this deficit continue for a sufficiently long period, then irreversible alterations of cerebral function will occur resulting in severe mental retardation.

Inadequate protein nutrition or synthesis or both during brain development could result in changes in function. If the degree of deprivation were suf-

ficiently severe and prolonged the changes in function might be permanent. Other experimental observations do in fact support this view that insufficient intake of protein during early neural development affects mentation. In rats and swine protein deprivation in early life not only causes behavioral changes but in addition also reduces the capacity to learn at a later age. Furthermore rats born of and suckled by malnourished mothers are deficient in their learning capacity. Germ free animals show the same changes so they cannot be blamed on infection.

In the human infant however protein-calorie malnutrition if severe enough produces two chemical conditions, infantile marasmus and kwashiorkor. Infantile marasmus occurs most commonly among babies weaned early without receiving suitable substitutes for human milk. This practice has resulted in a rapidly increasing proportion of children with severe protein calorie deficit.¹⁻³ Kwashiorkor is most commonly encountered in children who have not been weaned until the second or third year of life and had not received adequate food supplements. The diet therefore while it may be adequate in calories is grossly deficient in protein.

Apathy is universally present in these children. They lack curiosity, act sluggishly to a variety of stimuli. Similar apathy is found also in hospitalized malnourished children. As nutrition is restored so is the responsiveness to the environment. The electroencephalogram of the brain of protein malnourished children shows consistent abnormalities in the form, frequency, and amplitude and this also subsides when nutrition is restored. During recovery they grow first physically and with great rapidity. The child however never completely catches up with his healthy peers. The adult is significantly shorter than his healthy peers. The head circumference a useful but not absolute indicator of brain size is also smaller although its measurement is not necessarily related to variation in intellectual capacity.

Nevertheless the intellectual attainment of children who have recovered from a clinically severe episode of protein calorie nutritional deficit are consistently lower than those of individuals with adequate nutrition during infancy. These findings suggest that less severe and more chronic forms of malnutrition which do not result in dramatic life threatening nutritional diseases might contribute to the small stature universally observed among the economically poorer families of pre-industrialized

societies and might be correlated with a decrease in intellectual development.

It is clear that observations on animals and human infants suggest that malnutrition during a critical period of early life results in short stature and may in addition permanently and profoundly affect the future intellectual and emotional development of the individual.

L.H.N.

References

1. Eichenwald, H. F. and Fry, P. C.: Nutrition and learning. *Science*, 163: 664, Feb. 14, 1969.
2. Gordon, J. E.: In prevention of mental retardation through control of infectious disease. U.S. Public Health Service Publication No. 1692 (1968).
3. Eichenwald, H. F.: Nutrition learning and behavior. N. S. Scrimshaw and J. E. Gordon eds. (M.I.T. Press, Cambridge, Mass., 1968).
4. Nahum, L. H.: Nutrition of the fetus and the intelligence of the child. *Conn. Med.*, 33: 76, February 1969.
5. Platt, B. S., Heard, C. R. C. and Stewart, R. J. C.: Mammalian protein metabolism. H. N. Munro, J. B. Ellison eds. Academic Press, New York, 1964, Vol. 2.

Mutual Veterinary-Medical Problems: Developing Animal Models For Studying Human Diseases

Hypotheses about disease processes in man often cannot be tested directly. Experimental medicine is therefore heavily dependent on animal models. A good model adds new insight or a new dimension. There are negative models. For example the normal mink handles a certain virus well while the same virus produces a serious disease in the Aleutian mink. There are spontaneous models—"experiments in nature" collected from zoologists and zoos, biologists and veterinarians, animal colonies and field expeditions. There are orphan models, in search of a disease. The Rous sarcoma of chickens was a curiosity in 1910 but later revolutionized our thinking on cancer, virology, immunology and molecular biology.

The selection of the laboratory animal is one of the most important facets of an investigation in which living systems are necessary. The biological characteristics of the animal, its health genotype, susceptibility to natural diseases are often considered very casually or too late. A species in which one of its own natural diseases could be evoked on a predictable basis and which mimics some aspect of human disease has advantages which could outweigh all others in selecting it as the experimental animal. An elephant is obviously a difficult animal

to deal with but if it were the only animal in which a disease could be studied ways could be found to manage the elephant.

Fortunately nature is much more bountiful with disease states in smaller more manageable animals. Many animal disease models encompassing the whole spectrum of human diseases are known. Some have been carefully studied, others have only been described clinically or not at all. Unfortunately most of the pathological states which have been recognized in animals have thus far not been compared carefully with any human disease. It is true that many aspects of disease states can best be studied in man and should be. However, animal subjects do offer many advantages in controlled studies of the pathogenesis of disease, the interaction of genetic and environmental factors, recognition of physiological processes which are only made apparent by a pathological deviation, modes of inheritance and theories of etiology or new methods of treatment.

To provide a suitable animal model for the study of any pathological state, it is first necessary to identify and obtain at least one affected animal with the susceptibility or disease trait to be investigated. Then a breeding colony must be established to produce animals with the genotypes and phenotypes required. Such a breeding system has already been established for mice. Special veterinary and nursing care may be necessary to maintain some animals to reproductive age. For example a colony of dogs affected with hemophilia A, could only be developed following a system of careful nursing, banking blood for transfusions or other precautions to assure against loss of these animals from their bleeding tendency. And much else.

How is the diseased animal found to form the nucleus for such a colony? The largest reservoir consists of domestic animals, the first screening is usually in the veterinarian's office. Another source is among producing colonies of laboratory animals. Many fortuitous often accidental discoveries have been made in these situations. The most successful program so far involves mice especially the ones at the Jackson Laboratory in Bar Harbor, Maine where many excellent models have been developed. The mouse of course has some disadvantages as a model, its small size, restricted sampling of blood, difficult in clinical studies on individuals and in identification of individual chromosomes. They do however have a large number of mutants affecting the nervous system and well assembled genetic data.

A third possible source of new animal models could be among producing colonies, herds or flocks of domestic animals and poultry. There could include breeding establishments for sheep, cattle, dogs, cats, chickens, ducks and turkeys. Then there are the exotic animals in parks, zoos or in the wild that also offer some although less promising opportunities to find animal disease models. New species with value in the laboratory often come from studies of such animals from the wild state. There are also possibilities offered by fish hatcheries in which hundreds of siblings of the same age and genotype may be available for study.

For example the salmon is being studied for clues to life progression in man. The salmon's rapid degeneration from youth to old age starts almost from the moment the fish leaves the ocean to enter fresh water on the way to spawning grounds. In a period of two weeks the salmon deteriorates from beautiful shiny orange red creature to an aged rotting almost lifeless fish unable to combat infection, with circulation impaired and the skin peeling off. It appears this aging process is due to the pituitary gland which grows to four times normal size after the fish enters fresh water. There is a metabolic speedup in which the fat in the salmon's body was burned to almost nothing. Such a drastic change in metabolism could shed light on human metabolic processes. Another animal model is canine systemic lupus erythematosus having identical features in all respects to the human variety. The shell parakeet suffers from lipidosis and is becoming an excellent model for studying this disease in man. The desert sand rat is a wonderful model for studying human diabetes.

Jones lists over a hundred human disorders and finds animal models for each one of them. The skin, musculoskeletal system, respiratory system, cardiovascular system, hemic and lymphatic system, the gastrointestinal system, urinary, endocrine and nervous system, metabolic dysfunction and neoplasms. Bacteria and yeasts are good models for testing cancer drugs. Finally there are embryonal, fetal and pregnancy diseases with definite animal models for study.

Once an animal model is identified and at least a few living specimens are available then a facility is needed to develop the model to a point where it can be used in research. Several animal research centers are being developed in this country and are bringing together the necessary staffs to identify and produce animal models particularly those

which are genetically determined. The collaboration of many scientific disciplines including physicians, veterinarians, basic scientists and others is essential for success. Primate research centers now number seven in the United States.

The development of such animal and primate research centers should expedite the eventual understanding of disease processes in man as well as in animals, create new resources and approaches to the study of disease processes and create the model resources for those studies. We need intensified investigation of known animal diseases, meaningful comparisons with human disease and systematic searches for useful models among the animal populations. Special resources for these purposes should be developed in the interest of human welfare.

L.H.N.

References

1. Pathology Society Symposium. Fed. Proc., 28: 160-215, Jan.-Feb. 1969.
2. Jones, T. C.: Mammalian and avian models of disease in man. p. 162.

Protection Against Natural Aging By Antioxidants

Current theories of the cause of mammalian aging include loss of cellular programming, faulty copying in dividing cells and a variety of other cytogenetic or cytochemical aberrations. All of these call for a credible source of accumulating random damage—to DNA to lysosomes, to long-term low turnover colloids—which is partly though perhaps not wholly linked to metabolism. Because it can be slowed in rodents by calorie restriction, ideally this should look something like the damage done by sublethal irradiation.

Each hypothesis calls for some progressive molecular damage to provide the "clock" by which other mischiefs are timed. Molecular cross-linking on the model of collagen, but affecting more vital molecules has been a favorite hypothesis in some quarters and this is reinforced by the knowledge that chemicals can produce radiation-like life shortening and these are generally active cross-linking agents.

It is now suggested that the common feature of all these processes is that they are or can be the result of free-radical action. Free radicals arising in stored or long-term systems are the chief enemy for the preservation chemist whether he aims to preserve rubber from deteriorating, leather book bindings

from rotting when exposed to light, or broiler-chick feed from going rancid and losing its vitamin content. Of course, our bodies are self-renewing systems. However, if any of its reactive molecules are long-term, they avoid random deterioration from this cause only if they are specially protected. The rubber chemist delays the perishing of his product by the addition of specific anti-oxidants which scavenge the offending radicals particularly ozone and peroxides. The body may conceivably do the same through the action of—SH groups or special substances such as alphanatocopherol (vitamin E), but the protection may not be complete.

Some time ago Harman at the University of Nebraska began to examine the hypothesis that if radiation damage and aging were in any way analogous, then drugs which protect against radiation, might also protect against natural aging. His early experiments with anti-radiation drugs mercaptopyrimidines were positive, but non-toxic drugs were needed if they were to have clinical value. So this led to further experiments with non-toxic specific anti-oxidants. These materials were added in small amounts to animal food stuffs to reduce the rate of oxidative vitamin loss. Without them broiler-feed containing unsaturated oils loses vitamin E and A,

and the deficient feed may even cause direct peroxidative attack on brain lipids ("crazy chick disease").

The two materials most commonly used are B.H.T. and ethoxyquin. They are substances of low toxicity which are capable of scavenging free radicals both in stored feed and in the case of ethoxyquin in the hepatic circulation. Interestingly they are also used as rubber additives thereby establishing a common link between the processes of aging in human tissues and in man made materials such as rubber. The results of Harman's most recent experiments indicate a 30-40 per cent increase in mean longevity and a smaller gain in specific age in mice receiving 0.5 per cent B.H.T. in the diet and possibly an even larger increase in the case of ethoxyquin. The results are impressive to anyone who has even attempted to lengthen the life of a laboratory animal with a simple food supplement.

It is still possible that these results are in some way non-specific since the extreme maximum age reached was unaffected the main gain being in the period just presenile. This raises the question as to whether the "clock" of aging is being affected rather than some one pathological process. The logic of using anti-oxidants to protect cell constituents and delay age changes is attractive and will be more so if it can really be shown to work.

Some of the manifestations of aging particularly muscular deterioration has some resemblance to those of vitamin E deficiency. Nevertheless supplementation with this substance does not seem to correct them. It may be of course that the way vitamin E is given also prevents its absorption from the gastrointestinal tract. It is this fact that perhaps is responsible for the contentious nature of the literature linking vitamin E with antioxidant "police" activity and with the genesis of age pigment in cells. The source of this pigment (lipofuscin) seems to be lipid peroxidation and its site the surface of the lysosome.

The release of lysosomal enzyme particularly DNA is a hypothetical suspect both in carcinogenesis and in age damage to DNA in fixed non-dividing cells³ while damage to the lysosome membrane has been cited as a very probable effect of free-radical build up within the cell.¹ Thus we are clearly ready to test a hypothesis of aging with labelled chemicals. The reason is that unlike some past theories of aging this one opens the way for experimental verification. If non-toxic substances which resemble one another only in being active

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antioxidants can regularly prolong life both in mammals and shorter living aging systems such as the insect imago an important advance will have been made.

Our attention turns naturally to consider how such a finding could be tested to see if it might lead to prolongation of human life. Administration of large doses of antioxidants and restriction of free radical sources in the diet would have to be continued for 4-50 years before life table results like those in mice could be obtained for comparison. We might encounter a complication here because the unsaturated fats recommended by some to preserve the vascular integrity are themselves rich in free radicals.

Possibly one could look in the shorter terms for a slower rate of accumulation of chromosomal abnormalities in the treated group. A clear lead in life prolongation might be extremely difficult to test in man but if Harman's findings can be confirmed in other animals, there is a wealth of non-toxic antioxidant substances commercially available or to be developed.

L.H.N.

References

1. Slower aging. *Lancet* II: 1281, Dec. 14, 1968.
2. Nahum, L. H.: Vitamin E deficiency. *Conn. Med.*, to be published.
3. Nahum, L. H.: Biology of aging. *Conn. Med.*, 26: 259, April 12, 1962.

Human Ecology And The Doctor's Role

The newest branch of the Department of Health, Education and Welfare is the Consumer Protection and Environmental Health Service (CPEHS). This agency proclaims itself "the leading agency in the federal establishment to insure that our growing knowledge of both ecology and technology is vigorously applied to man's environment and the products he consumes."

CPEHS is a merger of Food and Drug Administration, National Air Pollution Control Administration and elements of occupational health, public drinking water, radiation protection units of the U.S.P.H.S. that had earlier been combined in the Environmental Control Administration. Its Chief is Charles C. Johnson, Jr.¹ who states that the first priority was to develop broad environmental criteria based upon our current understanding of human health and well being. No agency of government can singlehandedly design and build trans-

portation systems and cities and industrial plants. It cannot itself remove pollution from the air and assure pure drinking water and uncontaminated food. CPEHS cannot, he says, single handedly rebuild our ghettos or update our sewage systems or eliminate the noise and stress and crowding that mars the quality of our lives. But we can provide the focus on human health and welfare which is so essential to the attainment of these vitally important goals.

The chief of CPEHS states that it intends to become the spokesman not just for conservation or pollution abatement or food or drug protection or sanitation but for man—citizen and consumer. "We intend," he goes on to say "to become the advocate the spokesman for human ecological wisdom applied throughout our society." But first it must define that is a hospitable environment. To achieve this we must identify all that is injected into the air, the water, on the land or in the space we live in. It must examine and assess the impact on human health of whatever man puts into his environment individually and synergistically. It must be able to determine not only where they come from but why, what they do to the physical environment and how they affect man. To obtain this knowledge there must be a science base for CPEHS. With a science base the agency will acquire the ability to establish criteria and standards.

Crowding and congestion are pollutants of living space. It will be necessary to look at human beings as potential environmental insults. The agency must become capable of understanding contamination of space by humans as we are already able to understand contamination of the atmosphere or water by chemicals. The agency plans to investigate and develop criteria for density, crowding and congestion, especially since these aspects of our society have a wider effect on the environment than air pollution or water pollution. An increase in population density and industrialization that goes with it multiplies the contamination of air and water as well as producing its own pathology.

It will be a prime purpose of CPEHS to determine the relationship of human disease and social pathology to environmental deterioration. It will have to set up a national surveillance system to measure the gross physical impact of such deterioration. It will also have to study the tremendously important question of synergistic or additive effects of harmful environmental factors. It is obvious this

grand design will require scientists and administrators who will not be infiltrated from the selfish interests in our society whose aim might be to dilute or even vitiate the benefits to the citizen of the possible achievements of CPEHS. We have before us the dismal example of how water pollution control in Alabama was frustrated by agency inspectors who were actually representatives of the industry that were polluting the streams.² How to set up watch dogs to ensure that CPEHS branches actually are working in the interests of the public must continue to be an important concern of every citizen including the medical profession.

René Dubos is correct in emphasizing that the general worry about the environment has led us to concentrate on the social and biological dangers that man faces in the modern world. But there is more to human ecology than this one-sided view of man's relation to his environment. In the long run the most important aspect of human ecology is that all environmental factors exert a direct effect on the development of human characteristics in health as well as in disease. Just as we in medicine now identify health and sickness in individuals, the doctors of ecology will be attempting to identify the factors in society promoting societal health as well as those promoting societal illness and their consequences to be individual.

Thus the study of human ecology involves not only the immediate direct effects of environmental forces but also their indirect and long range consequences. How can such knowledge be obtained? Certainly not from over simplified biological systems. It will require the analysis of actual human institutions and the use of experimental models to reproduce some selected aspects of these situations. For human diseases there exist in the animal kingdom several species suitable for the development of useful models. What the experimental models might

be to study human ecology and societal diseases will be up to the "Doctors" of Society to develop. If the experimental method will be applied in human ecology there is no doubt that it can be readily developed into a flourishing experimental science.

The question is whether the scientific community is prepared to do human ecological research effectively. It will require the observations of the nature of societal institutions, how they function to create societal health and the circumstances in which they break down to lead to societal disease. It will also require observations upon human beings under a wide range of conditions. This will demand new kinds of research facilities. In theory such a science could be and should be developed within the University. However, Human ecology derives its importance from social concerns rather than from its relations to orthodox biological disciplines.

Dubos believes that for this science to develop, society will have to recognize that ecological knowledge is essential to its welfare. Then facilities for the procurement of such knowledge will be provided both outside the university complex as CPEHS will undertake to do and in new academic institutions not yet committed to the orthodox fields of science. No one can deny that potential does exist in the universities for studying the environment and how to direct it to the use of man. The function of such institutions will be to search for and advance knowledge in this area and train experts to pursue this same goal.

We physicians, however, must be clear about where we are in the human ecology scheme. We are not "doctors of society", its health or its disease. In fact there are no such as yet nor are there institutions for training such doctors. There are medical institutions developed to search for knowledge about human health and disease and to train doctors of medicine to deal with human illness. We are products of such an institution and our role is to maintain the health of the individual and to treat him when he falls ill. Confusion of roles can lead only to frustrations and failure.

L.H.N.

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References

1. Washington Science News: Seefuss a big job to do. Scientific Research, 4: 22, March 1969.
2. Nahum, L. H.: Curing the water pollution problem. Conn. Med., 30: 849, December 1966.

Attitudes Toward Computers Among Nursing Personnel In A General Hospital

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As part of a study of computer facilitation of psychiatric in-patient care two of the authors have described attitudes of hospital employees' and patients' attitudes toward computers.^{1,2} A further study described the changes in attitudes in student nurses before and after their exposure to the usefulness of computers in patient care.³ All of these studies took place at the Institute of Living, a private, non-profit psychiatric hospital. This report is an extension of these previous researches and entails an evaluation of the attitudes of nursing personnel at a general hospital. The hospital chosen for investigation was St. Francis Hospital also in Hartford, Connecticut and we assessed the attitudes of their nursing personnel prior to the extensive use of computers in the hospital. Our hypothesis was that our previous findings would not be unique to the setting chosen for study.

Method

In all of our series of studies we used a questionnaire developed by Kobler and modified by Reznikoff, Holland, and Stroebel. This questionnaire consists of 35 statements pertaining to the uses and potentials of computers, presented in random order which are to be rated on a scale from one to six. In order to prevent a response set, for some of the statements a rating of six indicates a positive attitude toward computers; in others it represents the most negative attitude. In scoring the questionnaire the scales are transposed where necessary so that higher ratings always reflect the more favorable attitude. Total scores for the 35 items range from 35 to 210 on a least positive to most positive continuum.

The subjects, all females, were 180 nursing students, licensed practical nurses, and registered nurses employed or in training at St. Francis Hos-

pital. They were instructed to complete the forms anonymously but were asked to indicate their age, education, duration of employment, marital status, department, and position in the hospital. Biographical data was complete except for two subjects who did not furnish any education information or indicate the department where they worked, while one subject failed to show her position in the hospital.

Results

The St. Francis Hospital nursing staff was divided into groups on the basis of each of the five demographic variables, examined separately. Using analyses of variance and t test techniques intergroup attitudinal comparisons were then done and the findings contrasted with the results of the attitude survey of Institute of Living nursing personnel.

As in the Institute of Living population, there was a borderline relationship between age and computer attitudes ($p < .10$) with those in their teens most negative in their feelings. Similarly duration of employment and marital status paralleled the findings of the previous study. The staff members of both hospitals who were employed for less than one year or more than ten years were less positive in their attitudes towards computers than those in the intermediary categories ($p < .05$). In both studies marital status was unrelated to computer attitudes.

Since only two of the St. Francis subjects had neither started college nor attended nursing school it was impossible to contrast high school graduates with those having more education as was done in the Institute of Living group. However, among the 178 subjects we again found that groups with increasing education showed a tendency toward a more favorable attitude toward computers than those with less education.

No significant differences were found in a direct comparison of the attitudes of the overall group of nurses at St. Francis Hospital and the total nursing

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group studied at the Institute of Living. The two student groups were most strikingly similar with mean attitudinal scores of 109.69 and 109.88 for St. Francis and the Institute respectively. In both studies the student nurses were significantly less positive in their attitudes toward computers ($p < .10$) than the more senior nurses.

Discussion

It appears that attitudes toward computers among hospital personnel are not materially influenced by the type of setting. Their attitude is more a function of their age, level of professional training and duration of employment at the particular hospital.

Again student nurses expressed the most negative attitudes toward computers. This finding need not be discouraging. In a previous study³ we showed

that when this group is exposed to some of the benefits of automated procedures they changed their attitudes substantially in a positive direction. In the sum, the results of the present research, in combination with prior studies, strongly suggest that computer attitudes are shaped by identifiable demographic variables which are not institution-specific and that these attitudes can be modified.

References

1. Reznikoff, M., Holland, C., and Stroebel, C. F. "Attitudes Toward Computers Among Employees of a Psychiatric Hospital." *Mental Hygiene*. 51:419-425, 1967.
2. Rosenberg, M., Reznikoff, M., Stroebel, C. F., and Ericson, P. "How Patients Feel About Computers." *Hospital and Community Psychiatry*. 334-336, Nov. 1967.
3. Rosenberg, M., Reznikoff, M., Stroebel, C. F., and Ericson, P. "Attitudes of Nursing Students Toward Computers." *Nursing Outlook*. 15:44-46, July, 1967.

Osler on Leukemia

Recovery occasionally occurs. A great majority of the cases prove fatal within two or three years. Unfavorable signs are a tendency to hemorrhage, persistent diarrhea, early dropsy, and high fever. Remarkable variations are displayed in the course, and a transient improvement may take place for weeks or even months. The pure lymphatic form seems to be a particular malignancy, some cases proving fatal in from three to eight weeks. In one of my cases the leukemia lasted between eleven and twelve years. . . . The longest course of my hospital series of the lymphatic type was three years, and of the spleno-myelogenous about the same duration. . . .

Fresh air, good diet, and abstention from mental worry and care, are the important general indications. The *indicatio morbi* can be met. These are certain remedies which have an influence upon the disease. Of these, arsenic, given in large doses, is the best. I have repeatedly seen improvement under its use. On the other hand, there are curious remissions in the disease, as mentioned above, which render therapeutical deductions very fallacious.

Quinine may be given in cases with a malarial history. Iron may be of value in some cases, as may also inhalations of oxygen. Treatment with the X-rays should be tried. Some observers have reported very good results. Personally, I have not seen any very striking improvement.

Excision of the leukemic spleen has been performed 43 times, with 5 recoveries.—Osler, W.: *Principles and Practice of Medicine*, ed 7, New York: D. Appleton Co., 1909, p. 738.

The Dream As A Diagnostic Aid In Physical Diagnosis

Harry A. Savitz, M.D.

"Dreams are the true interpreters of our inclinations, but art is required to sort and understand them."

Montaigne: Essays

"These whimsical pictures, inasmuch as they originate from us, may well have an analogy with our whole life and fate."

Goethe

"The interpretation of dreams is the royal road to our knowledge of these unconscious activities of the mind."

Freud

Freud, Jung, Adler, and their disciples have succeeded, in a measure, in deciphering the ephemeral, mystical language of the dream. Freud, for the first time, formulated the actual science of dream interpretation as an integral part of the psychoanalytic method. He and others have postulated that the dream protects the dreamer from awakening, and that outside events may be incorporated into the dream. But according to Freud's discussion, the mechanism of the dream consists of processes by which mental conflicts, wishes, anxieties, or other states find expression during sleep. The function of the dream is to disguise and distort in order to allow the continuance of sleep. In psychoanalysis these conflicts are traced back to an early or even an infantile period of life and later revived and brought into prominence in the consciousness of the dreamer. The unravelling and interpretation of these complex situations lie in the province of the Analyst. There are, however, instances in the experience of the Internist in which patients will reveal a dream involving a comparatively recent experience that is dramatized or symbolized in a manner not too complicated to lend itself to interpretation. There may be an external physical stimulus that disturbs the sleeping person, but the dream will disguise it so as not to awaken him. This may be illustrated by a situation

in which a student retiring very late sets his clock to awaken him at an early hour for his class. But as the alarm clock rings, he dreams that it is Sunday and he is hearing the church bells chime and he continues to sleep undisturbed; or there may be an internal and somewhat painful experience that might interrupt his sleep and the dreamer again dramatizes the episode in a manner that permits him to sleep. Not every dream is so intricate or complicated that elaborate analysis is required.

In the search of proper diagnosis one may find the dream to be a diagnostic aid. The dream may direct us to the vital organs that are involved in the symptoms of the patient, so that the physician may concentrate his search in that area; or if the physical examination is essentially negative, the dream may help to explain the patient's signs and symptoms of psychic origin.

The dreams in the following cases bear witness to Freud's comment that the function of the dream is to protect the sleeper from being disturbed by stimuli that otherwise might awaken him. This is accomplished by a process of distortion whereby the real meaning of the dream is disguised from the dreamer; a dual process which Freud calls plastic representation, including symbolism and dramatization. The images of the dream are symbols which use the subconscious thought of the dreamer.

Now in medical diagnosis, as in sleuthing in crime detection, every bit of evidence is helpful in determining the cause of a person's ailment. In the following situations the dreams of the patients were used as aids in diagnosing the illness.

A young man, 36 years old, white, unmarried, came into my office complaining of an occasional fluttery feeling in his stomach. In every other respect he felt perfectly well; he had just returned from a vacation in Bermuda. The evening before, while driving his car he became aware of this fluttery sensation. He said that he had not wished to disturb me that night and had consulted a neighborhood physician who prescribed a tranquilizer for him. He slept well that night except for a disturbing dream. He dreamt that he fell from a wharf in Bermuda and landed in the water

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between the wharf piles and a yacht that was moored alongside. The motion of the yacht squeezed him to the structure of the pier.

The resulting physical examination was essentially negative and on the surface did not indicate further study. But the vivid recollection of the details of his dream which had so disturbed him did concern me, and made me suspicious that they may have been due to some precoronary discomfort. I took an electrocardiogram and noted ST segment and T wave changes, suggestive of an acute myocardial infarction. He was referred to the hospital; diagnosis was confirmed and he was treated with coronary precautions. He made an uneventful recovery. I feel that in this case his dream was a clue that pointed to a coronary attack. In his sleep he was experiencing the painful symptoms of acute coronary insufficiency and the dream protected him from awakening.

On the other hand, the following situation demonstrates the dream as an aid to diagnosis in reverse—contrary to the patient's complaints of symptoms that he felt were due to damage to his heart, the dream pointed to a diagnosis of psychosomatic origin.

A man, 60 years of age, a lawyer by profession, came in to the office with complaints of palpitation, fatigue, nervousness, and fear that in his sleep he had suffered a "heart attack." The following is a digest of his story—he had been perfectly well the day before, pursued his daily routine with no sense of dyspnea or precordial distress. That night he went to bed at his usual hour, but later recalled that he had a dreadful dream that disturbed him, and on awakening he was trembling, his heart was "beating like a drum"—he had a sweat and was shivering with fear, believing that he had suffered a heart attack.

His physical examination was essentially negative; there was no change in his normal blood pressure of 130/70; his pulse was 64. An electrocardiogram was taken which was normal in all respects, and showed no changes from one taken previously in a routine physical checkup. Since there were no somatic signs to explain his symptoms, the details of his very disturbing dream were gone into thoroughly. Perhaps they would yield a clue to a psychic origin, and the following is a rather detailed report of his dream.

He was walking along a main thoroughfare with his chief in front of a large office building when he suddenly became paralyzed and could not walk any further. This dreadful episode caused him to awake from a deep sleep with great fear. Upon further questioning, he disclosed a number of important facts—the office building in front of which he was walking was the location of the office where-in he was employed. The patient was a graduate of a leading law school and had an M.A. degree. He was well thought of by the members of the firm in which he was employed; he had received small raises in salary from time to time, but his main duties continued to be routine, and he had not advanced to partnership in the firm. His chief, on the other hand, with only a A.B. degree, had been pushed ahead as the firm grew, and his salary had pumped accordingly.

From my knowledge and observations of this patient through the years I felt that he was, although obviously a good student of the law, inarticulate and lacked other qualities necessary for spectacular success in this field.

After some preliminary discussion, he was asked point blank, "Haven't you ever thought that in spite of having a higher degree than your chief you have not achieved his position nor his financial rewards?" He answered, "I have often thought that but kept these thoughts to myself." After some further discussion he began to accept the fact that scholarship alone could not bring him the results he desired.

I felt this situation was indicated in the dream in which he became "paralyzed" as he walked with his chief. He was assured of his good physical condition and that in my opinion there was no heart involvement to account for his symptoms. After some consideration of my interpretation of the sign of his distress, he seemed to find the explanation satisfactory and has continued to be in essentially good condition.

Summary

The two cases reported demonstrate that the dream can be an important aid in physical diagnosis—it can serve as a clue leading to the etiology of the patient's ailment. Verily did an ancient rabbi say, "A dream not interpreted is like a letter unread." (Rabbi Hisda: Talmud Brochat 552)

Hydromyelia In Von Recklinghausen's Disease With Neurofibrosarcoma

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The association of syringomyelia and von Recklinghausen's disease is well documented, yet the incidence of hydromyelia in neurofibromatosis is extremely rare. Furthermore, despite the rather frequent occurrence of malignant change in von Recklinghausen's disease, no case of hydromyelia in a patient with a neurofibrosarcoma complicating von Recklinghausen's disease can be found in the literature. The purpose of the present paper is to record such a case.

Report of A Case

S. B. was a 40 year old female with von Recklinghausen's neurofibromatosis. The disease had not appeared in other members of her family. Early in its course, her illness was of a mild nature. The patient married and led a relatively normal life until her first pregnancy at age 30 in 1957. At the time of delivery dystocia, produced by multiple uterine leiomyomata and retroperitoneal neurofibromata, necessitated a Caesarian section; however, the child was born without injury and is alive and healthy. In 1958 the patient underwent excision of uterine leiomyomata and benign retroperitoneal neurofibromata. In 1964 she had a large plexiform neuroma removed from the right buttock. In early Spetember, 1967 she was hospitalized with a five day history of cough and dyspnea. A chest x-ray revealed multiple large pulmonary nodules. Lung biopsy of the left lower lobe was interpreted as a neurofibrosarcoma. Other diagnostic studies included an intravenous pyelogram which demonstrated bilateral hydroureters and a large pelvic soft tissue mass.

The patient entered the Yale-New Haven Hospital late in September, 1967 for evaluation and treatment. Physical examination included normal vital signs. She was anxious and appeared acutely ill. Multiple café-au-lait spots and pedunculated tumors were widely distributed over the skin. A large firm subcutaneous mass 18x20x25 cm. was palpated in the right buttock. The skin over the lesion was darkly pigmented. No cardiomegaly or cardiac murmurs were present. The left lung base was dull to percussion and on auscultation diminished breath sounds and râles were noted in the same area. The abdominal examination was noncontributory. A large mass adjacent to the right adnexa was discovered on pelvic examination. Neurologic evaluation was within normal limits.

Among the pertinent laboratory findings were albuminuria, pyuria, and a peripheral blood leukocyte count of 19,250. Urine culture subsequently yielded *E. coli*. Repeated blood cultures were sterile. The urinary tract in-

fection was treated with Ampicillin. Radiographic study of the chest disclosed rapid progression of the intrathoracic disease process. During the next two weeks the patient received three courses of Cytosine arabinoside-C with little effect. Because of a decrease in hematocrit and platelets, chemotherapy was discontinued and packed erythrocytes were infused. Respiratory distress supervened, complicating a worsening urinary tract infection. During the fourth week of hospitalization, the patient suffered a cardio-respiratory arrest from which she did not recover.

At autopsy innumerable café-au-lait spots were evident. Multiple pedunculated neurofibromas were present on the skin, particularly on the face and chest. These tumors averaged 4 mm. in greatest dimension. The ungual regions appeared normal. A large glassy white neurofibrosarcoma measuring 30x20x20 cm. and weighing approximately 3.5 kg. occupied the right buttock. Microscopically, the neoplasm resembled a neurofibroma in some places. In many regions, however, there was no recognizable pattern of growth and the tumor invaded the surrounding tissues. The tumor cells were haphazardly arranged in sheets and clusters. They were extremely variable in size and shape. The cytoplasm was eosinophilic and generally sparse. The nuclei were round to fusiform in shape and hyperchromatic. Many bizarre giant nuclei were present. Mitoses were abundant (Fig. 1). Numerous regions of necrosis and

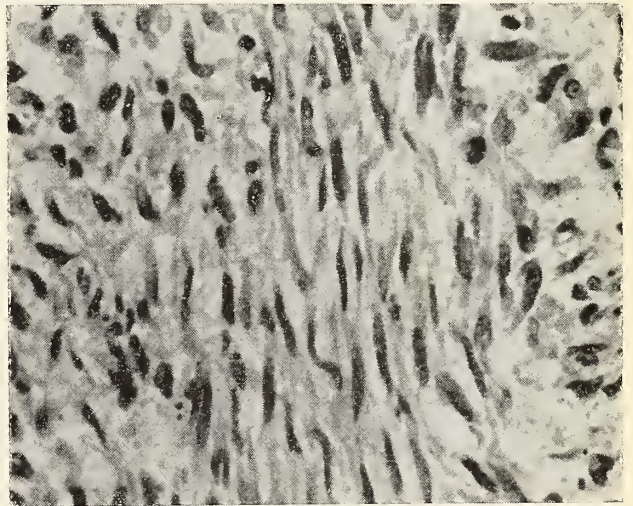


Figure 1

Neurofibrosarcoma. High power view showing pattern resembling neurofibroma with many fusiform shaped cells and a mitotic figure in upper right. Hematoxylin and eosin, X900.

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hemorrhage were scattered throughout the tumor mass. Each pleural cavity contained 100 cc. of serosanguinous fluid. Numerous metastatic neurofibrosarcomatous nodules were located in the lungs and on the superior surface of the diaphragm. There was biventricular dilatation of the heart. Acute passive congestion of the spleen and liver was prominent. The cortical surfaces of both kidneys were finely scarred due to moderate arteriosclerosis. The ureters were markedly dilated but there was no evidence of infection. The bladder was dilated and contained many diverticula. An acute hemorrhagic cystitis was present. Post-mortem blood and urine cultures yielded *E. coli*. Despite the dilatation of ureters and bladder, no evidence of mechanical urinary tract obstruction could be found. In the uterus, which was approximately three times normal size, several large intramural leiomyomata were discovered.

The brain and the entire spinal cord were available for neuropathologic examination. After fixation in 10% formalin for 7 days the following gross observations were made. The brain weighed 1575 gm. The leptomeninges were thin and translucent. Multiple coronal sections of the cerebrum at 6 mm. intervals revealed moderate edema as evidenced by a collapse of the ventricular system and a narrowing of the sulci. The arteries at the base of the brain as well as those within its substance were minimally involved by arteriosclerosis. No gross lesions were seen in the cerebrum, cerebellum or brain stem. On external examination the spinal cord was not enlarged in diameter. Multiple cross-sections of the cord revealed a central cavitory lesion which was continuous throughout the thoracic and lumbar regions, but was more pronounced at the thoracic level.

Blocks of tissue from the frontal lobe, temporal lobe including Ammon's horn, parietal lobe, basal ganglia, mesencephalon at the level of the red nucleus, medulla, cerebellum and spinal cord were embedded in paraffin, sectioned, and stained with hematoxylin and eosin, Nissl (thionin), Schroeder (myelin) and Holzer preparations.

Microscopically, anoxic change as reflected in a loss of neurons in the Purkinje cell layer and the dentate nucleus

of the cerebellum was noted. No other regions of the brain, including the Ammon's horn configuration, showed anoxic lesions. In fact, no other lesions were seen in the cerebrum, cerebellum or brain stem.

Serial cross-sections of the spinal cord disclosed hydromyelia most evident in the thoracic region. The hydromyelic cavity was lined throughout its course by a single layer of ependymal cells. In a section of the thoracic spinal cord a single small focus of ependymitis granularis was seen (Fig. 2). Surrounding the hydromyelic cavity was a band of swollen astrocytes. Gliosis was not observed elsewhere in the cord. No tumors were present within the substance of the cord or in the spinal canal.

Discussion

The classical features of neurofibromatosis were described by von Recklinghausen in 1882. Since 1910 the association of von Recklinghausen's disease and syringomyelia has been recognized.¹ Yet very few cases of hydromyelia have been described in patients with neurofibromatosis. A careful search of the literature disclosed only six such cases, the majority of which were associated with intramedullary tumors.²⁻⁷ Moreover, no instances of hydromyelia in cases of von Recklinghausen's disease with neurofibrosarcoma have been recorded.

Bielschowsky considered syringomyelia and hydromyelia as separate entities, the latter—which he termed “true syringomyelia”—having an ependymal lining.⁸ The author agrees with Bielschowsky in distinguishing the two conditions. Although in individual cases differentiation may be difficult, in general certain features of hydromyelia tend to place it in a category apart from syringomyelia. Syringomyelia, which is characteristically a linear cavity located dorsal to the central canal with its long axis perpendicular to the A-P plane, occurs most frequently in the third and fourth decades, usually produces definite clinical symptoms, and is most common in the cervical cord. Hydromyelia, a uniform dilatation of the central canal oriented in no particular plane, tends to occur at a younger age, to be asymptomatic, and to have no special affinity for the cervical cord.

According to some investigators, notably Hosoi, the incidence of malignant transformation in cases of neurofibromatosis is as high as 13%.⁹ While this figure is undoubtedly too generous, the occurrence of sarcoma in von Recklinghausen's disease is well established. However, due to the paucity of cases of hydromyelia associated with von Recklinghausen's disorder, it is not surprising that other cases of hydromyelia in association with neurofibrosarcoma have not been described.

Since 1950 in addition to the present case, seven cases of von Recklinghausen's disease have come to

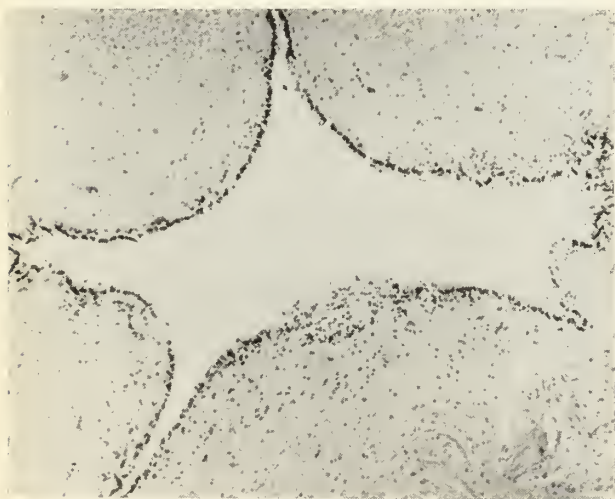


Figure 2

Thoracic spinal cord. High power view of hydromyelic cavity showing complete ependymal lining of cavity and small zone of ependymitis granularis anteriorly. Hematoxylin and eosin, X100.

autopsy at the Yale-New Haven Hospital. In none of these cases was there syringomyelia or hydromyelia. In one, the disease was complicated by a neurofibrosarcoma which originated in the right forearm and metastasized to the lungs and brain.

Summary

The occurrence of hydromyelia in a 40 year old woman with von Recklinghausen's disease who developed a neurofibrosarcoma of the buttock which metastasized to the lungs and diaphragm is reported. Hydromyelia in contrast to syringomyelia rarely occurs in von Recklinghausen's disease, and when seen usually is in association with an intramedullary tumor. No intramedullary tumor was found in the present case. While the occurrence of neurofibrosarcoma in von Recklinghausen's disease is not uncommon, the combination of von Recklinghausen's disease, hydromyelia, and neurofibrosarcoma is unique.

References

1. Maas, O.: Beitrag zur Kenntnis der Recklinghausenschen Krankheit. *M Schr. Psychiat. Neurol.* 28: 167-186, 1910.

2. Kernohan, J., and Parker, H.: A case of von Recklinghausen's disease with observations on the associated formation of tumors. *J. Nerv. Ment. Dis.* 76: 313-330, 1932.

3. Martz, L.: Neurofibromatose des sympathicus mit ungewöhnlicher Beteiligung des Rückenmarks, Gehirns und der Hypophyse. *Frankfurt. Z. Path.* 46: 119-139, 1933.

4. Hoerner, G.; d'Andrade, C.; and Basow, R.: Etude anatoclinique d'un cas de neurofibromatose du tronc et des membres. *Encephale.* 31: 124-135, 1936.

5. Gagel, O.: Neurofibromatose. In: *Handbuch der Neurologie.* XVI. O. Bumke and O. Foerster, eds. Berlin, J. Springer, 1936; pp. 289-318.

6. Slaczka, A.: So-called neuro-epitheliomas of brain and spinal cord; pathogenesis of syringomyelia, hydromyelia and neurinomatosis. *Neurol. Pol.* 19: 287-290, 1936.

7. De Busscher, J.; Scherer, H.; and Thomas, F.: Recklinghausen's neurofibromatosis combined with true syringomyelia. *J. Belge Neurol. Psychiat.* 38: 788-802, 1938.

8. Bielschowsky, M., and Unger, E.: Syringomyelie mit teratom- und extramedullärer Blastombildung zur Kenntnis der Pathogenese der Syringomyelie. *J. Psychol. Neurol. (Lpz.)* 25: 173-218, 1920.

9. Hosoi, K.: Multiple neurofibromatosis (von Recklinghausen's disease) with special reference to malignant transformation. *Arch. Surg.* 22: 258-281, 1931.

Lagging Research on Delayed Sensitivity

Despite its obvious importance in disease and medicine, or perhaps because of recent recognition of it, delayed hypersensitivity only lately has begun to be something more than a biologic phenomenon engaging primarily the thoughts of immunologists and of allergists with special interest in it.

Why has research on delayed (cellular) hypersensitivity lagged so much behind that on immediate (humoral antibody) hypersensitivities when its importance is at least as great? Progress in studies of allergy has depended upon both interest and availability of investigative techniques. For example, in forms of allergy related to anaphylaxis, the prototype of immediate hypersensitivity, neither has been lacking; anaphylaxis is readily induced and conveniently studied and, indeed, has been regarded by both allergist and immunologist as a convenient tool for analysing not only allergy but also antibodies, antigens, and antigen-antibody reactions. Although progress toward elucidating the mechanisms and significance of atopic hypersensitivity in disease has not lacked the spur of interest, it has been stymied technologically, so that contemporary understanding of it is far inferior to that of anaphylaxis.

Until recently, research on delayed hypersensitivity has had neither the advantage of incentive nor that of technical facility. Although some improvement of experimental techniques now makes it a less difficult subject to investigate, recent discoveries of its functions in disease probably have supplied the strongest motivation for current evident rapid growth of interest in it.—Crowle, A. J.: *Delayed Hypersensitivity in Health and Disease*, Springfield, Ill: Charles C. Thomas, Publisher, 1962, pp. xi-xii.

Scintillation Scanning In A Community Hospital: A Review

Chester Kay, M.D.

Modern day scanning was born in 1950 when Cassen et al¹ developed the scintillation crystal. Almost another decade passed before improvements in equipment and radiopharmaceuticals permitted the broad application of radioisotopic scanning techniques to nonresearch centers. In the last few years the introduction of newer radio-nuclides and more sophisticated equipment has opened new vistas. The principles and applications of scintillation scanning and particularly some of the recent developments in the field will be discussed in this series of papers.

General Principles

When an isotope is concentrated in an organ, some emitted gamma rays strike a thallium activated sodium iodide crystal producing flashes of light or scintillations. The crystal is surrounded by metal shielding which protects it from outside radiation. A collimator may focus at a given depth on the organ of interest. The scintillations from the crystal are converted to electrical impulses in a photomultiplier tube. The strength of the impulses are proportional to the energy of the gamma ray striking the crystal.

Most medically usable isotopes have their own characteristic gamma ray or rays with specific energy levels. The scanning machine has a pulse height analyzer and discriminator that allow only the gamma rays of the isotope of interest to pass through to the recording system and be counted while eliminating all rays of different energy levels. In a conventional scanning system when enough counts are monitored, the cathode ray tube produces a light which strikes the photographic emulsion of an x-ray film producing the photoscan. Simultaneously, a dot is produced on paper giving us the dotscan. The latter may be recorded in color.

Since a single view usually takes 20 minutes or more, dynamic studies have been limited. With

the introduction of technetium 99^m, a short-lived radionuclide which emits a low energy gamma ray, higher doses of radioisotope can be administered to the patient with less whole body radiation dose. The higher count rate has many advantages. It can be utilized to do more views and scans can be performed more rapidly.

Perhaps more important with the introduction of gamma cameras and high speed rectilinear scanning systems, scans can be done in seconds to minutes. In these systems large flat crystals are used. Each system has modifications in circuitry from the basic scanner permitting the information to be reproduced on either an oscilloscope or on magnetic tape and from these onto Polaroid film. With the use of scintiphotography dynamic function studies can be performed. Although in infant stages, this may be to scintillation scanning, what fluoroscopy is to diagnostic radiology.

Digital systems which are computer compatible can be incorporated into some equipment giving the numerical count rate over areas of interest in an organ or over an entire organ in addition to the picture printout mentioned above. This can be used to pick out areas of increased or decreased activity that the eye cannot see.

Brain Scanning

Scanning of the brain provides the clinician with a simple, safe, screening method for detecting intracranial pathology. The rationale is based on the concentration of a radioactive isotope in and around a lesion in comparison to normal surrounding tissue. The relative difference in concentration between the lesion and normal tissue is called the tumor to brain ratio. Even before the development of modern scanning techniques the localization of radioactive isotopes in brain lesions was appreciated and utilized both preoperatively and at the time of surgery.²

The number of radioisotopes used for brain scanning is extensive and will not be reviewed here.³ The agents currently used most are radioactive mercury labeled chlormerodrin, technetium

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99m pertechnetate and iodinated human serum albumin. Technetium 99m has to be eluted from a generator daily. Its short six hour physical half-life permits the use of larger doses with consequent higher count rates over the calvarium. Scan speeds can thus be increased permitting more rapid evaluation of the more difficult patient. Mercury-203 has a long 46 day physical half-life and a convenient 277 Kev gamma ray, but the dose to the patient is higher than with mercury-197 or technetium 99m . The target organ for radiomercury is the kidney. The use of mercurhydrin prior to injection of the radiomercury reduces the renal dose. The whole body dose from 10 millicuries of technetium 99m pertechnetate is 100mr. Positron emitting isotopes are being evaluated. Their role is to be established.

The mechanism by which radionuclides are concentrated in a brain lesion is not clear. Breakdown of the "blood brain barrier" occurs but the site or sites of localization of the isotope have not yet been defined.⁴

Technique: We generally start scanning the patient one-half hour after the intravenous injection of technetium 99m pertechnetate or two and one half hours after the injection of radiomercury. Technetium 99m may be given orally in which case the scan is started at one hour.

Earlier scans may be useful when a vascular malformation is being considered, and delayed scans helpful where metastatic tumors or other suspicious areas of pathology are suspected on initial views.⁵ Subdural and epidural hematomas may be seen to better advantage on delayed studies where the count rate of the normal vascular rim has decreased and more isotope has accumulated in the lesion itself.

The normal anatomy (figure 1) has been described elsewhere.⁶ When using technetium 99m pertechnetate, one must be aware of several artefacts which may interfere with interpretation.⁷ The scan should precede angiography to avoid possible artefacts. If angiography is done first it is preferable to wait two days before scanning the patient.

Clinical Applications: Several extracerebral entities may produce abnormal areas of increased activity (hot spots) on the scan. Edema or hemorrhage into the soft tissues may be confused with a subdural hematoma both of which appear as a hot peripheral "vascular rim" (figure 2). Clinical history and followup are important in the differential diagnosis. Osseous lesions such as Paget's disease, primary or secondary tumors, fibrous dysplasia and

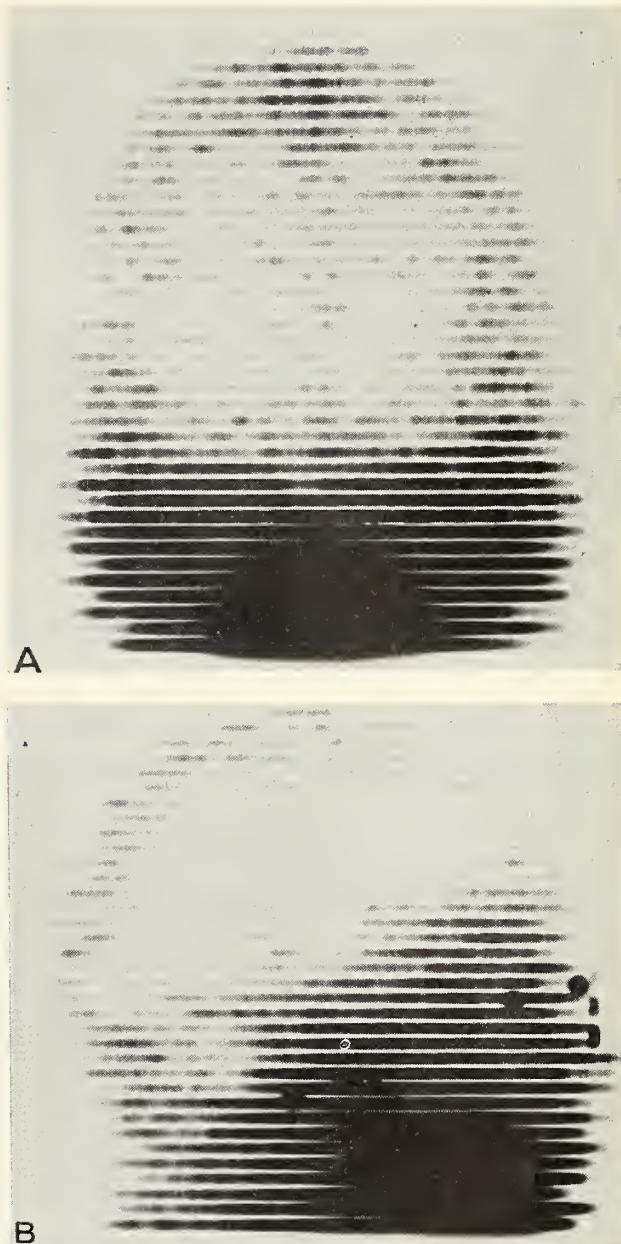


Figure 1

Normal brain scan using technetium 99m pertechnetate a) anterior projection, b) lateral projection.

inflammatory disease can mimic peripheral brain lesions. Scanning with radiostrontium will differentiate osseous from soft tissue and intracerebral pathology. Routine skull films may be of help.

Brain scanning has enjoyed its greatest applicability as a simple safe screening procedure after careful clinical evaluation raises the question of an intracerebral lesion. The false positive rate should be low. False negatives do occur especially in posterior fossa tumors or tumors near the temporal muscles such as pituitary lesions. The ac-



Figure 2

Chronic subdural hematoma. Mercury 203 brain scan showing localized peripheral pickup on right side in anterior projection.

curacy of brain scanning in detecting intracranial tumors is about 80 per cent.⁸ Maximum accuracy is obtained with supratentorial meningiomas and glioblastomas. It may be less with slow growing astrocytomas and subtentorial lesions. If there are definite neurologic signs in the face of a negative scan, further evaluation in the form of arteriography or pneumoencephalography should be considered. These procedures complement scanning. Occasionally lesions may be visualized on the scan and not be appreciated on an arteriogram or pneumoencephalogram.

Primary tumors (figure 3) appear as a single hot spot. Brain contusion, inflammation, and vascular

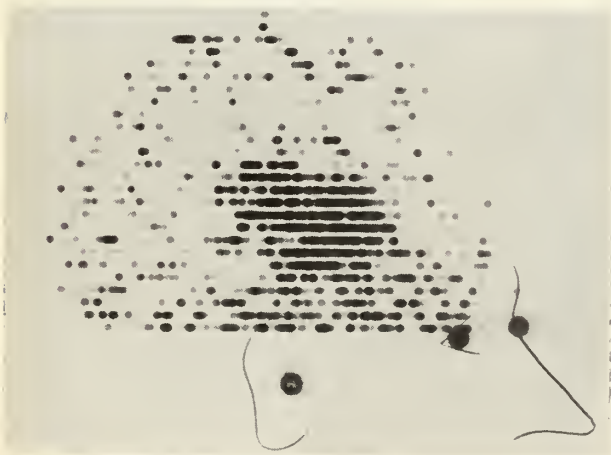


Figure 3

Glioblastoma Multiforme. Mercury 203 brain scan showing hot spot in the lateral projection.

lesions, such as arteriovenous malformations, may have a similar appearance, particularly if the latter bleeds. Thus the scan does not give histology. Metastatic disease must be considered when more than one hot spot is present. The scan may depict more lesions than the angiogram particularly if the lesions are small and vascular or when they are so placed that they counteract each others vascular displacement.

Another situation where scanning is of value is in the unconscious patient or in one who is suspected of having a sudden cerebrovascular occlusion. In the stroke patient the scan is usually negative for ten days to two weeks. It then may become positive (figure 4). A brain tumor or subdural hematoma will be depicted during this period. The

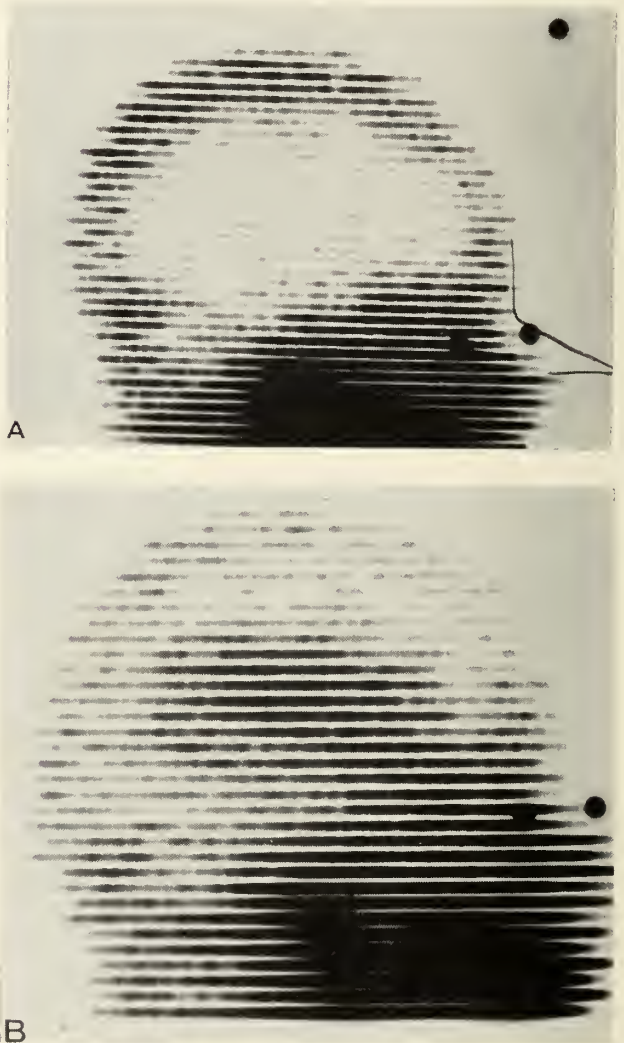


Figure 4

Stroke. a) Right lateral technetium 99^m pertechnetate scan is normal two days after sudden right sided weakness. b) repeat scan 14 days after onset shows pickup in distribution of middle cerebral artery.

brain scan may remain positive for two to three months in some patients following a cerebrovascular accident and then will become negative, whereas brain tumors remain static or increase in size. Rapid sequence scanning using the gamma camera after a stroke can demonstrate decreased blood supply to the involved area.

Another application is in the situation where followup of a lesion is desired postoperatively or after radiotherapy. Here repeat arteriography can be avoided. Sufficient time must be allowed for edema and other changes to subside before repeating the study.

If a subtle lesion is suspected on the scan, repeat examination at a later date using another isotope may be helpful.

Vascular Pool Scanning

Rejali, MacIntire and Friedell¹⁰ described heart pool scanning in 1958. They used the idea that if one of the blood's normal constituents could be tagged, pools of blood in large vessels or the heart could be visualized on a scintillation scan. ¹³¹I labeled human serum albumin was the agent first employed. ¹³¹I iodipamide sodium delivers a lower whole body dose due to its rapid clearance by the polygonal cells of the liver. Although not approved for general use at the time of this writing technetium 99^m labeled human serum albumin seems to be even more preferable.¹¹ Indium 113^m is also being evaluated.¹²

The two major applications of vascular pool scanning are: 1. the differentiation of pericardial effusion from cardiomegaly, and 2. the differentiation of large vascular masses from other lesions.

Heart Pool Scanning: When one of the radioiodinated compounds is used, the thyroid gland should be blocked with 10 drops of Lugol's solution before and after the scan. The distribution of radioisotope in the heart, aorta, and frequently the proximal pulmonary arteries will be visualized on the scintigram. The photoscan is superimposed on a six foot antero-posterior chest film taken in a neutral phase of respiration. The maximum transverse diameter of the heart pool is measured and is divided by the maximum diameter of the cardiac silhouette on the roentgenogram. The ratio is 0.80 or more in normals, or with effusions of less than 100 cc. It is less than 0.80 with effusions greater than 200 cc.¹³ Accuracy holds in both hypertrophied and dilated hearts. Other helpful signs are separation of the vascular heart pool from pick-up in the liver and lungs. In pericardial effusions,

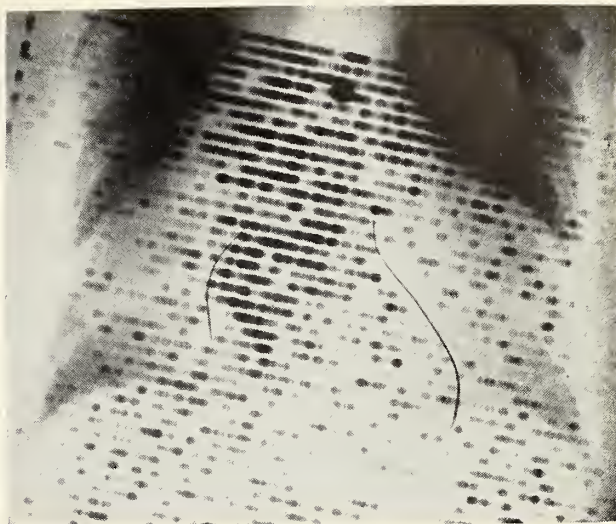


Figure 5

Pericardial effusion. Note diffuse separation of isotope in vascular pool of the heart from the outer margin of the cardiovascular silhouette. The scan is superimposed on a chest x-ray.

the separation of the vascular cardiac pool from the outer borders of both sides of the cardiac silhouette is symmetrical. Localized defects in the vascular pool of the heart may represent an intracardiac thrombus, tumor or ventricular aneurysm.

Differentiation of Mass Lesions: If the question arises as to whether a mass near the heart, hilum or the aorta is vascular or represents a tumor, a heart pool scan may be helpful. The isotope will collect in blood vessels (e.g. aneurysms or a tortuous aorta) whereas the tumor will appear "cold" on a superimposed roentgenogram. If the aneurysm appears partially filled, a clot within it is probably present. Thus one may avoid an unnecessary arteriogram by a completely benign procedure.

The examination also can be carried out where an abdominal aortic aneurysm is suspected. Anterior and lateral scans are necessary to differentiate a tortuous aorta from aneurysmal dilatation.

Recent Developments: With the introduction of the Anger camera, isotopic angiography has become practical. An intravenous bolus of technetium 99^m pertechnetate can be injected and scans done every few seconds over the vessels of interest.¹⁴ The technique has been used to demonstrate blood flow in the brain, carotid arteries, heart, pulmonary vessels, lungs, kidneys, and abdominal aorta. Thus vascular occlusion, aneurysm of the aorta, and many other circulatory abnormalities can be easily, rapidly, and safely screened or diagnosed in minutes with a minimum of discomfort to the pa-

tient. To date, however, conventional arteriograms must be considered definitive.

Newer instrumentation and isotopes promise the ability to perform even more rapid scans and thus greater dynamic work with isotopes.

Myocardial Scanning

Scanning of the myocardium in cases where myocardial infarctions are suspected but not verified by electrocardiography can be carried out with cesium 131. The normal myocardium picks up the isotope whereas the infarcted area appears "cold". The scans appear to correlate well with coronary arteriograms, although best in normals and those with lesions of the left coronary artery.¹⁵

Thus the role of scanning in the evaluation of cardiovascular disease is growing rapidly. The simplicity and safety of scanning procedures accompanied by good accuracy makes them diagnostic and desirable. In the more experimental areas such as isotopic angiography it is still wise to perform an arteriogram for the definitive diagnosis, particularly if surgery is contemplated.

Acknowledgment

My appreciation to Mrs. Mary Stephenson without whom this paper would not have been possible.

Bibliography

1. Cassen, B., Curtis, L., and Reed, C., A sensitive directional gamma ray detector, *Nuclonics*, 6:78, 1950.
2. Moore, G. E., Use of radioactive diiodofluorescein in the diagnosis and localization of brain tumors, *Science*, 107:569, 1948.

3. Wagner, H., Radioisotope techniques in the diagnosis of diseases of the central nervous system, *Rad. Clin. N. Amer.* 4:203, 1966.
4. Freeman, L. H., Schneider, J. A., Kay, C. J., Zingesser, L. H., and Zimmerman, C., Role of Scintillation scanning in clinical medicine, *N.Y. State J. Med.*, 66:2020, 1966.
5. Miller, M. S., Simmons, G. H., Optimization of timing and positioning of the technetium brain scan, *J. Nuc. Med.*, 9:429, 1968.
6. Mack, J. F., Webber, M. M., and Bennett, L. R., Brain scanning; Normal anatomy with technetium-99^m pertechnetate, *J. Nuc. Med.*, 7:633, 1966.
7. Witcofski, R. L., Roper T. J., Maynard C. D., False positive scans from extracranial contamination with technetium-99^m, *J. Nuc. Med.*, 6:524, 1965.
8. Witcofski, R. L., Maynard, C. D., Roper, T. J., Comparative analysis of accuracy of 99^m Tc-pertechnetate brain scan: Followup of 1000 patients., *J. Nuc. Med.* 8:187, 1967.
9. Rosenthal, L., Detection of altered cerebral arterial blood flow using technetium-99^m pertechnetate and the gamma-ray scintillation camera, *Radiology*, 88:713, 1967.
10. Rejali, A. M., MacIntire, W. J., and Friedell, H. L., A radioisotope method of visualization of blood pools. *Am. J. Roent.* 79:129, 1958.
11. Bonte, F. J., Radioisotope blood pool scan, *Am. J. Roent.* 96:690, 1966.
12. Potchen, E. J., Adatepe, M., Welch, M., Archer, E., Struder, R., Indium In¹¹³ for visualizing body organs, *JAMA*, 205:208, 1968.
13. Sklaroff, D. M., Charkes, N. D., and Morse, D., Measurement of pericardial fluid correlated with the I-131 Cholografin and IHSA heart scan, *J. Nuc. Med.*, 5:101, 1964.
14. Rosenthal, L., Applications of the gamma-ray scintillation camera to dynamic studies in man, *Radiology*, 86:634, 1966.
15. Collier, R. E., Matson, J. L., Tomme, J. W., and Hyland, J. W., correlation of myocardial photoscanning and coronary angiography in angina pectoris, *Radiology*, 91:310, 1968.

Research and Teaching

So deep may be the absorption in the problems of disease that the virtue of teaching, . . . the patient line-upon-line, precept-upon-precept method becomes a burden. . . . The patient demonstrator who spends two hours with a group of students . . . has a place of equal importance with the man who is chasing the secret of anaphylaxis. . . . A man who is not fond of students and who does not suffer their foibles gladly misses the greatest zest in life; and the teacher who wraps himself in the cloak of his researches, and lives apart from the bright spirits of the coming generation, is very apt to find his garment the shirt of Nessus.—Osler, W.: *The Pathological Institute of a General Hospital*, reprinted; *Glasgow Med J* pp. 10-11, (Nov.) 1911.

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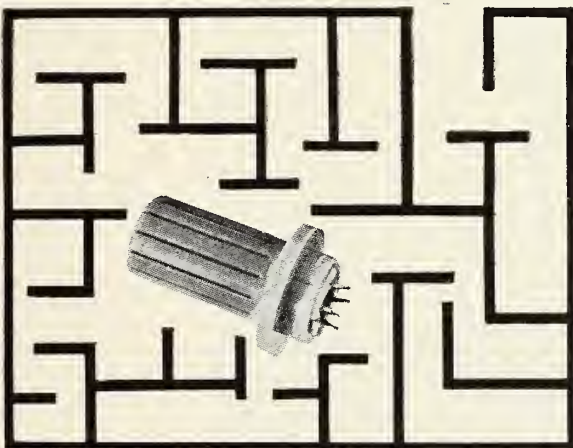
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University of Wisc., B.A., 1927; M.A., 1928; Ph.D., 1930; M.D., 1935

University of Wisconsin and Medical School Positions—1926-1936

Albany Medical School

Associate Professor of Physiology and Pharmacology, 1936-39

Rotating Internship—Wisconsin General Hospital—1936-36

Residency at Bellevue Hospital

U.S. Army Medical Corps (Colonel, M.C., USAR)

Tilton General Hospital, Ft. Dix, N.J., 1941-46

Graduate of Command and General Staff Course-1956—Retired 1966

Present Location & Position

St. Francis Hospital, Hartford, Conn. Director, School and Dept. of Anesthesiology from March 1, 1946

President-Medical-Dental Staff 1967-68

Member:

Society of Exp. Biol. and Medicine, 1930-present

American Physiological Society, 1932-present

American Medical Association, 1935-present

American Society of Anesthesiologists, 1939-present—President 1954

Connecticut State Society of Anesthesiologists, President, 1947

New England Society of Anesthesiologists, President, 1953

Academy of Anesthesiology, President, 1963-64

Connecticut State Medical Society, 1946-present; President-Elect 1968

Hartford County Medical Association—Member 1946-present

President, 1960

Councillor, 1963-present

Hartford Medical Society—1949-present

President, 1963

Board of Trustees—1969

Editorial Board of *Anesthesiology*, 1956-64

Board of Trustees of Anesthesiology Foundation 1956-present

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Member-Board of Trustees-Wood Library-Museum, 1963-present

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STEVENS J. MARTIN, M.D.
President

THE PRESIDENT'S PAGE

Service to mankind is the outstanding attribute of the medical profession. It was well expressed by Dr. Charles H. Mayo, who once stated that "all who have benefited from community life, especially the physician, owe something to the community." The opportunity to serve is a common daily experience and one given to all physicians. But to serve as your president is not only an honor but also a privilege and an obligation. To all, during my tenure, I pledge my utmost efforts to measure up to the high standards set by my predecessors and to work for improvement of the health care of the people of Connecticut.

The President's Page serves many functions. Aside from the chance for commenting on actions taken by the AMA, our House of Delegates, the Council and Standing or Special Committees, it also gives the president an opportunity to share his reflections with you on medical trends and progress both here and abroad. However, both reports and reflections depend basically, if not entirely, on *communication*. And communication must of necessity be a "two-way" street. *In short*, let me hear from you often.

It is presumed that our membership knows its officers and Council representatives. What is conjectural, however, is how many know of the many Standing and Ad Hoc Committees whose dedicated efforts are in constant demand. Elsewhere in this issue of our Journal is the list of these Committees whose function, and at the least whose chairman, should be known to all.

Committees vary in function, composition, complexity, and as to time of their "peak activity." As of this writing, while the State Legislature is in session, the State Legislative Committee has been virtually staggered by the many urgent, often unexpected, demands made upon its members. Contact with key leaders and members of the legislature, participation at hearings, and preparation of rebuttals or alternate proposals are but few of the many obligations of this Committee. Know these colleagues and be prepared to help them when asked. Often there is no substitute for prompt action.

From time to time, one is approached by a member who has a desire to serve on a state committee. This desire is not only laudable and indicative of a healthy trend but must not be ignored. Surely many of you have attributes and capabilities, sometimes dormant and unexpressed, that would be valuable to the activities of at least one of our numerous committees. Why not let us know—especially if you are in doubt as to your potential. Your participation is vital to our strength and continued progress. Remember, this is *your* Society and we need you.

STEVENS J. MARTIN, M.D.

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Associate General Manager

SUMMARY OF ACTIONS

COUNCIL MEETING

Wednesday, March 19, 1969

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Weber, Jr., Brandon, Dean, Bradley, Rogol, Cramer, Farrell, Petrie, Spitz, Purnell, Shepard, J. M. Grant, Nemoitin, Johnson, Friedberg, R. F. Grant, Pelz, Granoff, Wilson, Palomba and Roch.

Also present were: Mrs. Lindquist, Dr. Hess, Dr. Patterson, Dr. Pasquariello, Dr. Goldstein, Mr. Donelan (AMA), Mr. Villano and Dr. Richards.

Absent were: Drs. Grendon, Abbot, Fabro, Egan and McDonald.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of February 27, 1969.

Election of Student Members

It was VOTED to elect to Student Membership the following residents of Connecticut who are enrolled in medical schools in the United States:

James E. Cox, 330 Carol Road, Stratford
University of Rochester—Class of 1972

Pre-Med: Harvard College

Parent: Stuart T. Cox

Richard B. Everson, 93 Mullen Hill Road,
Waterford

University of Rochester—Class of 1972

Pre-Med: Trinity College, Hartford, Conn.

Parent: George A. L. Everson, Sr.

Harry V. May, Jr., 1951 Burr Street, Fairfield

University of Rochester—Class of 1972

Pre-Med: Georgetown University

Parent: Harry V. May, Sr.

Date of Next Meeting

The date for the next meeting of the Council was scheduled for Thursday, April 17, 1969.

III. Old, New and Special Business

Communication—Ad Hoc Committee to Study Group Practice

In response to a letter from the Chairman of this Ad Hoc Committee, James H. Root, Jr., in which Dr. Root expressed doubt that the Committee of three members could do an adequate job of pursuing the study of group practice "in-depth" unless substantial staff assistance was furnished, it was VOTED to request the Ad Hoc Committee to develop and submit a *modus operandi* for pursuing the study, included estimates of staff requirements, anticipated costs, goals, etc.

Communication—Chairman, CSMS Section on General Practice

At the invitation of the Council, D. William Pasquariello, Bridgeport, Chairman of the CSMS Section on General Practice, joined the Council to elaborate on the letter he had recently written to the Chairman of the Council in which he expressed certain dissatisfactions with the role currently being played by General Practitioners in the administrative and policy-making functions of the Society. Following a fruitful period of discussion, in which it was agreed that there should be continuing communications between all concerned with promoting the high purpose of the Society effectively, the Council VOTED to accept Dr. Pasquariello's views as information and to thank him for bringing them to the attention of the Council members.

Completion of Report of Nominating Committee

The slate of nominees for the PR Committee was completed, completion having been held over from the February 27 meeting at the request of NHCMA representatives. A motion to reconsider the February 27 nomination for the office of Vice-President failed to receive the required two-thirds vote.

A motion to approve the slate, as amended, as-a-whole was carried by a roll call vote of 19-3. Those voting "nay" were Drs. Dean, Bradley and J. M. Grant.

**Discussion—Legislative Efforts re Medicaid
“Usual and Customary Charges”**

In accord with a recommendation made by the Committee on State Legislation, Max R. Goldstein, Hartford, had been invited to join the Council to elaborate on certain thoughts he had advanced at the Legislative Committee meeting with respect to “saving” the usual and customary charge program for Medicaid in the next biennium. Following a lengthy and critical discussion of Dr. Goldstein’s proposal in relation to all other facets of this question, the Council VOTED to adopt the following motion:

IT IS MOVED: That the chairman appoint an Ad Hoc Committee, the membership to include, among others, Max Goldstein, chairman, Cramer, Friedberg, Gardner, Granoff and Polivy, such Ad Hoc Committee to develop a specific program (Legislative Proposal) based, in general, on the material submitted to the council by Dr. Goldstein, and from this program to proceed through legislative and political channels, as may be appropriate, to seek enactment of legislation by the General assembly which will preserve the principle of “usual, customary and reasonable charges” as the method for payment for physicians’ service under Medicaid in order to continue and augment the improving medical care to beneficiaries and to conserve state funds.

**CSMS Contribution to Twenty-Fifth Anniversary
of Woman’s Auxiliary**

Having been apprised of plans being made by the Woman’s Auxiliary to CSMS to hold a luncheon program in celebration of the Auxiliary’s twenty-fifth anniversary of its founding, the Council VOTED unanimously to approve the recommendation of the Fiscal Advisory Committee that the sum of \$500 be contributed to the Woman’s Auxiliary to be used to help defray the costs of the anniversary program.

**Reports—Ad Hoc Committee on Guiding Principles
for County Review Committees**

It was VOTED to approve a two-part report submitted by this Ad Hoc Committee, and to recommend approval of both parts by the House of Del-

egates at the Annual Meeting. The first section of the report proposed certain revisions in the “Guiding Principles for County Review Committees”, adopted by the CSMS House of Delegates in 1965. The second section of the report made recommendations concerning the Society’s formal cooperation with private insurance carriers, on request, in the administration of “usual, customary and reasonable charge” programs, and outlined a mechanism for providing such cooperation.

**Resolution re Medicaid “Usual and Customary Charge”
Program**

It was VOTED to adopt a resolution on this subject as follows:

WHEREAS: Legislation extending beyond March 1, 1969 the usual and customary charge concept of paying physicians for services rendered to Medicaid beneficiaries has not been enacted; and

WHEREAS: The Commissioners of Welfare, Finance and Control have, therefore, imposed a uniform fee schedule as the method of payment for such services; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society urge the Council nominated members of the Title XIX Medical Advisory Committee, the statutory authorization for which expired on March 1, 1969, to remain available to the State Commissioners of Welfare and of Finance and Control for consultation; and be it further

RESOLVED: That the foregoing action of the Council shall not be construed as abandonment of the Society’s support for continuation and/or restoration of the usual and customary charge concept of paying physicians for services rendered to Medicaid beneficiaries, but only as a service in the public interest.

N.B.: The foregoing is a summary of the proceedings and actions of the Council on March 10, 1969. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.

Placement Wanted

INTERNIST—33, Board eligible, subspecialty in Rheumatology, Connecticut license. Desires to locate in Connecticut and interest in practice either in association, group, hospital, student or employee health. Available Summer 1969.

GENERALIST—Age 62, desires position in Connecticut full time, 40 hours per week in hospital or emergency room service, or employees' clinic in industry. Connecticut license.

DERMATOLOGIST—31, Board eligible, presently completing residency. Available July, 1969. Has National Boards. Desires solo or group clinic-type practice. No present preference as to size of community.

Placement Opportunities

PRACTICE FOR SALE—Well-established practice in Internal Medicine available. Modern offices and laboratory, large practice. New Haven County.

WANTED—PHYSICIAN: Extensive general practice available due to death of physician. Sevenroom suite in new medical building, equipment and supplies. Reasonable terms. Groton-Ledyard area.

PSYCHIATRIST—Community-oriented mental hospital, to work in or direct 500-bed comprehensive mental health center, one of several units in a 1600-bed hospital. Opportunity for teaching, clinical work and research, also to work with or direct a team of social workers, psychiatric residents, psychologists, occupational therapists and approximately 190 nursing staff personnel. Opportunity for association with Wesleyan University, Yale and UConn. Qualified candidates may be considered for other senior staff positions. Liberal benefits with housing available at a nominal charge, annual leave to attend medical conventions. Send all particulars in first letter, including references, to Mehadin K. Arafeh, M.D., Superintendent, Connecticut Valley Hospital, Box 351, Middletown, Connecticut 06458.

OPENING FOR CHIEF OF MEDICINE in 496 bed State Veterans Hospital. Directs the program of medicine, plans, organizes and supervises case histories involving medicine. Must be Board eligible and be eligible for Connecticut license. Maximum age 65 years. Salary up to \$23,060 annually,

plus many fringe benefits. Quarters and services available at minimal cost. Write or call Personnel Officer, Veterans Home and Hospital, Rocky Hill, Connecticut, 529-2571, Ext. 395.

WANTED: Internist for General Medical and Surgical Accredited State Veterans Hospital. Duties are those of a ward officer on a general medical ward. Applicants must be Board eligible and up to 65 years of age, if still vigorous. Salary range: \$17,980-\$22,180. Many fringe benefits. Apply Personnel Officer, State Veterans Home and Hospital, Rocky Hill, Connecticut.

PHYSICIAN for Emergency Room in 90 bed community hospital in Central Connecticut. 40 hour week, week-ends free if desired. Full cooperation from panel of staff physicians who cover E. R. remaining time. Must be eligible for Connecticut license. About \$30,000 per year. Reply: Joseph Zimerman, M.D., P.O. Box 867, Meriden, Connecticut 06450.

PEDIATRICIAN—for a rapidly growing community in Western Connecticut. Present pediatrician wants to concentrate solely on subspecialty. Arrangements on solo, salary or associate basis.

OBS-GYN—Board certified OBS-GYN desires certified or qualified associate for a practice in small Eastern Connecticut town. Contact: Edmond B. Raheb, M.D., 14 Carter Street, Danielson, Connecticut 06239.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE GENERAL MANAGER'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

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New Rules of Ethics Adopted

In accordance with the Bylaws of the Society, Article X, Paragraph 7, Section c. (1), the Judicial Committee "may study and render an opinion, when indicated, on any question referred to it from the council . . . (and) . . . may use its judgment whether or not to request endorsement (of its opinion) from the Council for the purpose of establishing (an ethical) principle". When so endorsed by the Council, the Judicial Committee's decisions "become binding on all members of the Society".

On February 27, 1969, the Judicial Committee filed a series of its decisions with the Council which, having received the endorsement of the Council, are now rules of ethics binding on all members of the Society. The rules are as follows:

Relationships Between Physicians and Chiropractors

- (1) It is unethical for a physician (M.D.) to refer medical problems to a chiropractor.
- (2) Any referral of a medical problem by a chiropractor to a physician (M.D.) shall be treated by the physician as a referral of a medical problem from a lay person.
- (3) It is unethical for a radiologist (M.D.) to accept any referral from a chiropractor for his

services. He may not send any reports to a chiropractor, even if requested to do so by a patient.

Pre-Signing of Prescription Blanks

The practice of pre-signing prescription blanks to be left at pharmacies, nursing homes, hospitals and similar places shall be considered both unethical and unprofessional conduct on the part of a physician.

The Judicial Committee also notes that "being found guilty of such unethical and unprofessional conduct can lead to action by the Connecticut Medical Examining Board which may result in suspension or revocation of the physician's license to practice".

Medical-Legal Guide—Principles for Cooperation

The "Medical-Legal Guide", as amended by the Conference Committee with the Connecticut Bar Association on February 7, 1969, and the "principles" contained therein are binding on all members of the Society and infractions thereof are subject to disciplinary action. Members of the Connecticut Bar Association will be similarly informed. The full text of the revised "Medical-Legal Guide" follows:

Medical-Legal Guide—Principles For Cooperation

The Connecticut State Medical Society and The Connecticut Bar Association

Adopted by the Council, Feb. 27, 1969

Introduction

These principles are being promulgated with the hope that they will prove helpful to the members of each profession and the public they serve.

In recent years there has been an increasing number of cases requiring medico-legal testimony and there has ensured a need for improved and closer cooperation between the medical and legal professions.

A substantial part of the practice of law and medicine is concerned with the problems of persons who are in need of the combined services of a lawyer and a physician. Each must keep in mind

the differences in the capacities and characteristics of the practitioner of each profession and that, while law and medicine may each be termed a science, each is an inexact science and such inexactness is and always will be accentuated by the human limitations of its practitioners.

Purposes and Principles

These principles are based on the recognition of a bilateral responsibility for the solution of medico-legal questions and all matters of mutual interest to the two professions. Of fundamental importance is the acknowledgment of the duty the members owe the professions themselves and the public.

These principles are not rules and regulations but they are goals worthy of the aims of each profession. No set of principles can be so all inclusive as to define each and every detail of successful cooperation. Most situations will be amenable to each solution if the members of each profession always honor the lofty objectives sought by their respective professions. To implement this, local groups of doctors and attorneys should form joint committees to solve any local problems.

Both doctors and lawyers are bound by a code of ethics. The attorney is bound by the Canons of legal ethics to prosecute his client's cause as an advocate. Certain legal procedures are necessary to facilitate this.

A doctor has the obligation to treat the physical and mental welfare of his patient as a whole and to expedite his patient's recovery from illness in accordance with the code of medical ethics.

To implement this common cause, there are certain essentials to be recognized by both professions.

Physicians' Responsibility for Medical Records

- (1) The medical profession must keep adequate records in order to supply to a patient's attorney all information regarding the patient-client's medical history provided the physician has received proper authorization from the patient. For the patient's protection and for his own protection, under no circumstances is a physician to divulge a patient's medical record without the authorization of the patient or his attorney. Such information must be available to a patient or his attorney in litigation cases.
- (2) What Should be Included in a Treating Physician's Report—In writing the report, the following information should be included:
 - a. Date, time and place of first visit.
 - b. Brief history of accident (how it happened, not why); i.e., Patient fell down a flight of stairs landing on her back at the bottom of the stairway.
 - c. First Examination: Patient complained of low back pain, neck pain and in general areas over her entire spine, examination disclosed, etc.
 - d. Subsequent examinations and treatment showed what? Include continued complaints, therapy, referral to other doctors, and the time patient was able to work.
 - e. Diagnosis: Include injuries reasonably and probably received and any reasonably prob-

able effect the injuries received did have in the precipitation, aggravation and causation of any other injury or disease.

- f. Prognosis: The physician's opinion of disability, past, present and future, and the necessity of future medical treatment and surgery.
- (3) Physicians must recognize the importance of promptness in providing a patient's attorney with such information from his medical record that is essential in protecting the patient's legal rights. When the doctor provides a written report, the attorney shall be responsible to the doctor for a reasonable fee.
- (4) Report of the Independent Medical Examiner—It is the duty of a physician making an independent medical examination to evaluate the patient's condition, the etiology of the condition and a prognosis as respects the patient. Such physician, however, should avoid an inquiry into the liability aspects of the case; that is, a determination of who was at fault.

The Physician as a Witness

The physician in court is a witness and as such should not assume the role of the patient's attorney. The physician should be courteous to the cross-examiner whose function it is to ascertain the accuracy of the medical testimony. Attorneys, in turn, should recognize the physician as a witness and treat him with respect and consideration due an aide to the court in its attempt to reach justice. The physician should be guided by the thought that he is a consultant giving as accurate an opinion as he is capable of presenting.

Compensating the Physician

Under no circumstances should a physician enter into a financial agreement on a contingency basis. Whenever any collection of medical bills and expenses has been made pursuant to other insurance coverage, such as medical payments, accident-health insurance, Blue Cross, CMS, etc., the client should be advised by the attorney that such funds should be immediately sent to the doctors whose bills have been submitted.

Where, prior to settlement, the client is in the financial position to pay the medical bills, he should be urged by his attorney to do so forthwith. If the client is unable to do so, the doctor should seriously consider foregoing any action for the

collection of his bill before the termination of all litigation.

It is recommended that the patient authorize the lawyer to pay the physician directly out of any recovery which may be had in a particular law suit once settlement has been made. It is the attorney's obligation to provide for payment of the physician's services out of such settlement proceeds. It should be held professionally reprehensible for an attorney to make settlement of a case without providing for the physician's services if he has made an agreement with the physician witness with the client's approval.

It should be held professionally reprehensible for a physician to refuse to send out his patient's medical report to the attorney because his medical bill for services rendered has not been paid up to that time.

In the event the patient-client has a disagreement concerning his physician's charges, and the attorney has collected funds by way of a settlement or judgment, such attorney shall request permission of his client to hold the amount of the doctor's bill until the doctor and patient have resolved their disagreement. This provision does not, however, prevent the doctor from executing assignments with his patients, which assignments, upon delivery to the attorney, shall be recognized by the attorney.

An Attorney's Responsibility

It is improper for an attorney to seek to color the professional opinion of the physician contrary to the ethics of both professions. Such is beneath the dignity of each profession.

At the inception of the case, it is the obligation of the attorney to advise his client that regardless of the outcome of any litigation the client will still be legally responsible for the payment of all reasonable medical bills incurred, and all reasonable disbursements made by the attorney in the prosecution of the case.

Whenever the attorney and the patient are of the opinion that a consultation with another doctor is advisable, the attending doctor should be consulted and such doctor should do all necessary to cooperate.

The client should be advised that the physician is entitled to reasonable compensation for a pretrial conference and for his appearance in court, and the attorney will personally guarantee the doctor's fees for time spent on pretrial conferences. Advising the client to give reasonable compensation for the doctor's time in court shall be the responsibility of the attorney.

Doctor-Lawyer Conference

Under circumstances which require it, every effort should be made to arrange a pretrial conference between the physician and the attorney in order to prepare properly for trial. During the conference the attorney should acquaint the physician with what will be expected of him in court and the physician should take this opportunity to review the patient's medical history with the patient's attorney.

The Subpoena

A subpoena is used to enforce a person's attendance at court. The voluntary appearance of a person at court obviates the necessity for a subpoena.

Even though the court rules require the issuance of a subpoena for any medical witness, doctors and attorneys should cooperate so that subpoenas become unnecessary. So far as possible, the doctor should make himself available for testifying upon reasonable notice. The attorney should cooperate by notifying the doctor and in calling him so that the doctor's attendance would be with the least amount of inconvenience to his schedule. When it appears that the voluntary appearance of a doctor cannot be procured, then a subpoena should be issued. These provisions shall apply to both the attending and examining physician.

Dermatologic Side Effects of Psychotropic Drugs

William S. Appleton, M.D., Richard I. Shader, M.D.
Alberto DiMascio, Ph.D.

The majority of prescriptions presently written in the United States aim to alter not the patient's physical state but his emotional state. This effort to calm the excited and activate the depressed with the new psychotropic drugs has flourished within the past fifteen years. Considering the widespread use of such agents—chlor diazepoxide is the largest selling prescription drug in this country—the number of serious side effects encountered has been remarkably small.

With the exception of very rare severe allergic reactions with skin manifestations (exfoliative dermatitis, angioneurotic edema) and the slightly more common gray and purple skin pigmentations occurring after years of phenothiazine therapy, skin side effects are usually not serious. Nonetheless they are common, can be alarming in appearance, and present interesting problems in diagnosis, prevention, and management.

Psychoactive agents produce a wide variety of skin conditions, which can be divided into "simple allergic" and "light-related" reactions. The "simple allergic" conditions will be considered first.

Simple Allergic Skin Reactions

A maculo-papular rash on the face, neck, upper chest and extremities occurring between fourteen and sixty days after initiation of drug therapy is the most common allergic skin reaction. It is estimated to develop in 5 to 10% of those receiving chlorpromazine, for example, varying slightly if at

all with dosage level.¹ While such allergic reactions have been reported following most psychotropic drugs, chlorpromazine is the most frequent offender. Diphenhydramine hydrochloride or other antihistamines may be given for relief of itching. ACTH has also been effective in more serious cases.² It is often not necessary to interrupt drug therapy, but if it is then the drug may be resumed once the rash has subsided, usually without recurrence.

Occasionally angioneurotic edema or infrequently exfoliative dermatitis develops. These may endanger life,³ and require vigorous management such as "aerosols, epinephrine, cortisone and other supportive measures".⁴

Light-Related Skin Reactions

A photo-allergy is not an alteration in reaction to light *per se*, but to substances rendered allergenic by the electro-magnetic energy of wave-lengths in the general range of the visible to ultra-violet spectrum. Brodie⁵ notes that light energy captured by the drug electrons becomes great enough to break chemical bonds and the resultant free radicals cause tissue damage. He postulates that the free radicals in some way form a true allergy.

Estimates of frequency of photosensitivity to phenothiazines vary from 20% to 60% or more.⁶ Gambos and Yarden report 21%,⁷ Prien and Cole 22%,¹ Tredici et al.⁸ report "two out of three patients", but they seem alarmist. Chlorpromazine causes the most photosensitive reactions, while recent evidence suggests that thioridazine does not produce any, even in "massive" doses.^{9 10} Duration of therapy with chlorpromazine seems to be a crucial factor. Most cases have developed in patients receiving chlorpromazine for four to eight years at doses from 500 mg. to 1500 mg. daily.^{11 12} Recently, Korenyi¹¹ has demonstrated the protective value of benzophenone lotion as a sun screen against ultra-violet irradiation, suggesting that this compound is an effective treatment in cases of phenothiazine-induced photosensitivity.

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DR. RICHARD I. SHADER, Assistant Professor of Psychiatry, Harvard Medical School; Lecturer in Social Relations, Harvard University; Senior Research Psychiatrist and Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center.

ALBERTO DiMASCIO, Ph.D., Research Associate in Psychiatry, Harvard Medical School; Co-Director, Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, Boston, Mass.

Pigmentation

Slate gray to metallic purple skin pigmentation confined to body areas exposed to sunlight (face, neck, limbs) is a rare side effect which appears only after years of phenothiazine treatment. Chlorpromazine definitely produces this discoloration,^{10 13-15} but none of the phenothiazines can be said with confidence not to do so.¹⁶ Skin pigmentation usually occurs in conjunction with corneal and lens opacities. Thus, eyes should always be examined when skin pigmentation is observed.

Ban and Lehmann¹³ hypothesize that chlorpromazine causes

... a shunting of dopa metabolism away from epinephrine synthesis, (resulting in) increased melanin formation, which beyond a certain level (facilitated by light) may become exhausted, and the excess melanin pigment which is dropped from the epidermis into the dermis may then form a complex with the excess of chlorpromazine. (We suggest) that this complex is the (blue) pigment.

Using the dopa, epinephrine and melanin hypothesis, they go on to relate hyper-pigmentation to some of the other well-known side effects of chlorpromazine such as extra-pyramidal symptoms and orthostatic hypotension. They suggest that an interference with dioxyphenylalanine metabolism leads to all these side effects.

The frequency of this bluish pigmentation is about 1%¹³ but may increase as chlorpromazine use continues. The incidence varies with size of dose and duration of therapy, with risk increasing in high-dose, long-term treatments, especially in women.¹⁷

Greiner, Nicolson and Baker¹⁴ tried an inhibitor of melanin synthesis (D-penicillamine) and darkness and found that D-penicillamine was effective in depigmentation when subjects were not receiving chlorpromazine concurrently, and that in mild cases seclusion from light alone was effective. Gibbard and Lehmann¹⁸ also found D-penicillamine and avoidance of direct sunlight to be effective.

In a previous paper we discussed the effects of phenothiazines and other psychotropic drugs on the anterior pituitary,¹⁹ pointing out how such drugs may block the release of prolactin inhibitory factors. It is of interest that melanocyte-stimulating hormone (MSH), although not secreted by the anterior pituitary, is also under the tonic inhibitory control of the hypothalamus. This may account for the areolar pigment changes which often accompany galactorrhea. Blockade of MSH inhibitory factor may also contribute to the pigmentation changes

observed with long-term, high-dose phenothiazine administration.

Discussion

The incidence of skin reactions to psychotropic drugs is extremely difficult to determine. A great problem exists in differentiation of the false from the true drug side effect. For example, we have reported on five dramatic young female in-patients who complained within a brief span of time of alleged chlorpromazine skin rashes, all of which proved not to be drug-induced.²⁰ Prien and Cole¹ in a study of high-dose phenothiazine reported:

Allergic Reactions	High Dose N=117	Low Dose N=113	Placebo N=111
Skin rashes	2%	3%	3%
Photosensitivity	3%	2%	3%

This table underlines the importance of careful baselines and the need to establish the incidence of placebo side effects before estimating the incidence of drug-induced adverse reactions.

Summary

Simple allergic skin reactions are idiosyncratic, not preventable, and usually not serious. They can be treated with antihistamines or ACTH and only rarely cause the interruption of drug therapy. Occasional serious reactions include angioneurotic edema and exfoliative dermatitis. Sunburning can be severe and is preventable by changing to a drug not associated with photosensitivity, by avoiding direct summer sun, and by use of lotions to absorb or block ultra-violet rays. Skin pigmentation may be irreversible and can be prevented by the obvious methods of keeping dosage (especially of chlorpromazine) to an absolute minimum, by the use of D-penicillamine, and by keeping the patient out of the light.

References

1. Prien, R. F., and Cole, J. O.: High Dose Chlorpromazine Therapy in Chronic Schizophrenia, *Archives of General Psychiatry* 18:482-495, 1968.
2. Kalinowski, O. B., and Hoch, P. H.: *Somatic Treatments in Psychiatry*, New York: Grune and Stratton, 1961.
3. Bare, R. L., and Harris, H.: Types of Cutaneous Reactions to Drugs, *Journal of the AMA* 202:710-713, 1967.
4. Lear, E.: *Chemistry and Applied Pharmacology of Tranquilizers*, Springfield, Ill.: Charles C. Thomas, 1966.
5. Brodie, B. B.: The Mechanisms of Adverse Reactions, *Third International Pharmacological Meeting* 4:39-40, 1966.
6. Satanove, A.: Pigmentation Due to Phenothiazines in High and Prolonged Dosage, *Journal of the AMA* 191:262-268, 1965.
7. Gombos, G. M., and Yarden, P. E.: Ocular and Cutaneous Side Effects After Prolonged Chlorpromazine Treatment, *American Journal of Psychiatry* 123:872-874, 1967.
8. Tredici, L. M., Schiele, B. S., and McClanahan, W. S.: The Incidence and Management of Chlorpromazine Skin-Eye Syndrome, *Minnesota Medical Journal* 48:569-574, 1965.

9. Leger, Y.: A Four-Year Appraisal of Thioridazine, *American Journal of Psychiatry* 123:713-718, 1966.
10. Barnes, G. J., and Cameron, M. E.: Skin and Eye Changes Associated with Chlorpromazine Therapy, *Medical Journal of Australia* 1:911-916, 1966.
11. Korenyi, C.: The Effect of Benzophenone Sunscreen Lotion on Chlorpromazine-Treated Patients, *American Journal of Psychiatry* 125:143-146, 1969.
12. Smith, Kline, and French Laboratories: Reference Manual: Fifth Edition, in *Ten Years Experience with Thorazine*, Philadelphia: Smith, Kline, and French Laboratories, 1964.
13. Ban, T. A., and Lehmann, H. E.: Skin Pigmentation, A Rare Side-Effect of Chlorpromazine, *Canadian Psychiatric Association Journal* 10:112-124, 1965.
14. Greiner, A. C., Nicolson, G. A., and Baker, R. A.: Therapy of Chlorpromazine Melanosis: A Preliminary Report, *Canadian Medical Association Journal* 91:636, 1964.
15. Zelickson, A. S.: Skin Changes and Chlorpromazine: Some Hazards of Longterm Drug Therapy, *Journal of the AMA* 198:341-344, 1966.
16. Dancel, A. B.: Intrathecal Trifluoperazine in Schizophrenia, *South African Medical Journal* 40:47-50, 1966.
17. Greiner, A. C., and Berry, K.: Skin Pigmentation and Corneal and Lens Opacities with Prolonged Chlorpromazine Therapy, *The Canadian Medical Association Journal* 90:663-665, 1964.
18. Gibbard, B. A., and Lehmann, H. E.: Therapy of Phenothiazine-Produced Skin Pigmentation: A Preliminary Report, *American Journal of Psychiatry* 123:421-423, 1966.
19. Shader, R. L., and DiMascio, A.: Endocrine Effects of Psychotropic Drugs: I. Galactorrhea and Gynecomastia, *Connecticut Medicine* 32:106-108, 1968.
20. Appleton, W. S.: The False Drug Side Effect: Which Patients Complain? *British Journal of Psychiatry* 114:507-512, 1968.

Just Words

One of the masochistic pastimes of American medical men is to complain that American medical men write badly and that something should be done about it. Nobody will deny that better writing would be good, and I have no desire to be the nobody who does. But must we motivate our interest in ever-improved communication by repeating *ad nauseam* that nonsense American medical men write worse than their colleagues abroad and than their compatriots in other walks of life?

My editorial work for international medical congresses burdens my desk with medical manuscripts in French, German, Italian, Spanish, and of course English, but there appears to be no significant correlation of quality with either language or national provenance.

The problem lies elsewhere, as will be apparent when we note (and this is a fact) that learned writing a century ago was better on the whole than it is today. But even here I boldly assert that our best writers write as well as the best writers wrote a century ago. The trouble is simply that so much writing is needed that more people must write than can write. This is the same today all over the world, even in Britain.

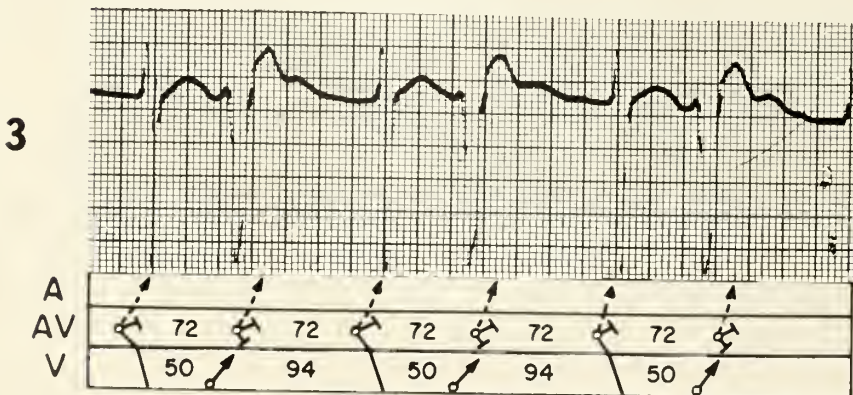
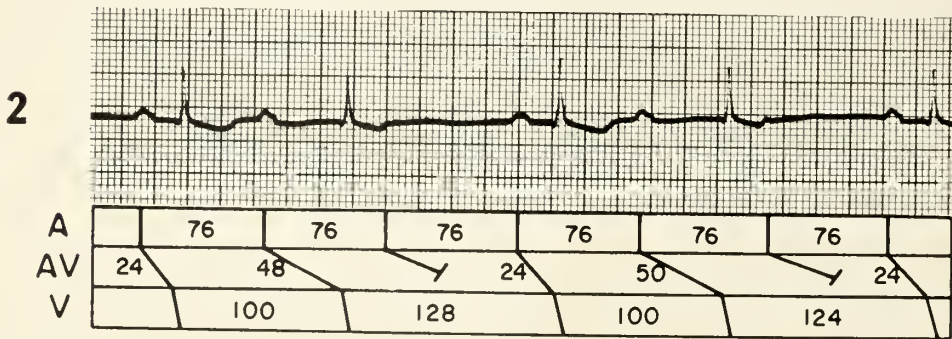
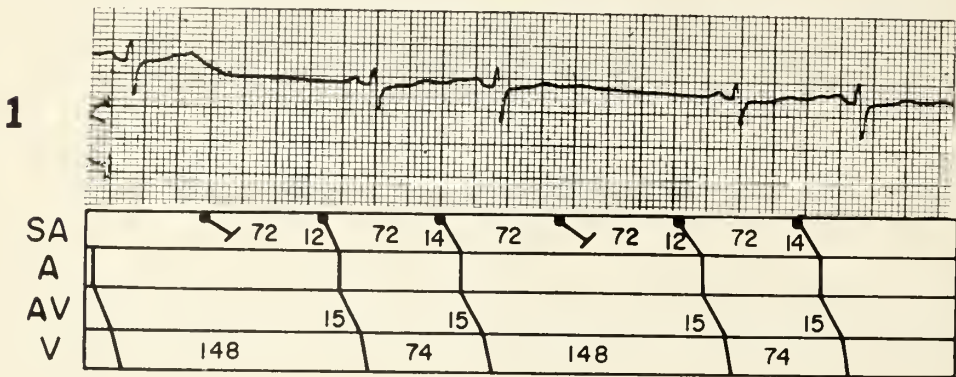
By way of a meek little footnote I will admit that one literary vice luxuriates more ridiculously in American medical writing than elsewhere. I refer to the extraordinary idea that an effective style can be achieved by an ample admixture of purple. The following (cross my heart) was not cooked up, but is a bona-fide quotation from a paper on osteoarthritis: "Waves from the rock dropped into the still clear pool, crumble the banks and roil the water until oil from improved circulation quiets the waves and filters the water."—Alexander Gode, Ph.D.

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Director—Department of Electrophysiology
Memorial Unit

Below are rhythm strips from three different patients. In each instance the ventricular beats are grouped in bigeminal fashion. Identify the underlying rhythm disturbance and its most likely cause.



The rhythm strips were recorded in three patients who were suffering from digitalis intoxication.

In the ladder diagrams on the previous page, S-A designates the sino-atrial node; A designates the atria; A-V, the atrioventricular node and junctional tissues; and V, the ventricles. Numbers refer to hundredths of a second.

1—Sino-Atrial Block with 3:2 Wenkebach Periods

Digitalis excess can delay or block conduction between the sinus node and the atria. Note that the pacemaker is in the S-A node and that the sinus discharge rate is 82/minute. The diagram assumes an 0.12 second initial conduction time between the sinus node and atrial muscle. The S-A conduction time of the second beat of each couplet is prolonged to 0.14 sec. Every third sinus impulse is completely blocked. This results in bigeminal grouping of both the atrial and ventricular complexes. When the sinus impulse is completely blocked, the pause that results is of such a length that the P-P and R-R intervals that contain it are exactly double the P-P and R-R intervals of the beats displaying normal sinus rhythm.

2—2nd Degree A-V Block with 3:2 Wenkebach Periods

Digitalis excess can delay or block conduction in

the A-V node and junctional tissue. Note that the pacemaker is in the sinus node and gives rise to an atrial rate of about 80/minute. The PR interval of the first beat of each couplet measures 0.24 seconds. The PR interval of the second beat measures 0.48-0.50 seconds. The next sinus beat depolarizes the atria but fails to be conducted to the ventricles. Since every third sinus impulse is blocked at the A-V junction, bigeminal grouping of the ventricular beat results.

3—A-V Junctional Rhythm with Ventricular Ectopic Beats

Digitalis excess may suppress the sinus node and an A-V junctional rhythm may then occur as an escape rhythm. Note that there are no P-waves in this tracing. They may be absent because of the presence of retrograde block from the A-V junction, or the retrograde activation of the atria may be occurring during the inscription of the QRS complex and thus not be visible. Coupled to each A-V junctional beat with a fixed coupling interval is a ventricular ectopic beat. The A-V junctional rate is 85/minute. Every other A-V junctional beat fails to elicit a ventricular response because of the refractory state in the ventricle resulting from depolarization by the ventricular ectopic beat.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

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CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

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NATIONAL BOARD PLANS FOR 1969-70

At the mid-winter meeting of the board of directors in Chicago, January 22 and 23rd, the program development committee recommended that the auxiliary continue its "accent on youth" in the coming year, broadening the emphasis to include the whole spectrum of family life . . . how individual family members relate to one another and to the community.

A second emphasis which the board approved was a focus on leadership within local communities in the field of health.

To help carry out these recommended emphases, it was decided that the committee on children and youth (a special committee for 1968-69) be designated a national program extension committee for 1969-70 with four regional chairmen who will work closely with state chairmen in this area.

The board members also felt that the campaign against provocative violence in TV and movies should be continued, stressing cooperation with other groups in a positive letter-writing campaign to policy makers in the entertainment industries, making explicit comments on specific TV and movie programming.

The program development committee pointed out that the White House Conference on Children and Youth is scheduled for 1970 and suggested that local auxiliary members participate as individuals in study and action groups preparing for the conference.

In regard to the role of doctors' wives as community leaders concerned with local health-related issues, Mrs. John M. Chenault, president-elect and chairman of the program development committee stated: "Sometimes we feel that health care is being taken over by either government agencies or volunteer health organizations, but this is simply not true. In any community, be it a bustling met-

ropolitan area or a rural hamlet, there are unmet health needs, either in actual service offered or in ability to make these services available to those who have need of them. What more challenging opportunity for a local auxiliary than to find that need and do its part in helping to meet it!"

The board noted that though physicians are being urged to take a leading part in "Comprehensive Health Planning," their role will be limited by the terms of the law (PL 89-749). "Physicians' wives as individuals may be of assistance here," Mrs. Chenault pointed out, "if they are asked to represent volunteer organizations on local planning groups. In any case, we need to be kept informed as to the ramifications of PL 89-749, a law which will have great impact on the future of health care services in this country and thereby will inevitably affect the medical profession."

The board re-affirmed the importance of health education efforts. The ten package programs developed by the national auxiliary should continue to be an effective means of reaching community groups, such as PTA's, church groups, women's clubs and students groups with reliable health information. These programs will be reviewed and up-dated by national chairmen in the coming months.

A recurrent theme in board discussions of health care and its delivery was the shortage of health personnel. "County auxiliaries have a commendable record of support for both AMA-ERF and health careers activities," Mrs. Chenault stated, but we need to increase our efforts in both these areas.

The Connecticut Quarterly is published four times a year by the Woman's Auxiliary—CSMS for its members. The present editor, Mrs. Norman H. Gardner of East Hampton, and circulating editor, Mrs. F. Erwin Tracy of Middletown, share the task



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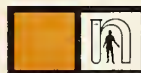
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of accumulating and editing material of interest to the members and arranging for the publication and distribution of the newsletter. A glance through each issue will tell you that every phase of auxiliary work is covered during the year. Introduction of state officers, reports of the AMA convention, fall conference, and regional workshops are a part of the year's report. The county presidents are presented during the year, and the county accomplishments are honored. Connecticut can be proud of *The Quarterly*.

AROUND THE STATE

New Haven County

Board of Governors

New Haven County Medical Association

February 20, 1969

A meeting of the Board of Governors of the New Haven County Medical Association was held on Thursday, February 20, 1969 at the Colonial House, Hamden, Connecticut.

After the usual order of business, reports were read from the various committee chairmen.

Our Councilor, Stewart J. Petrie, reported that the vacancy in the office of vice president of the Connecticut State Medical Society will be left open for the remainder of the term in deference to the memory of Max Caplan, deceased. The Council was brought up to date on the status of bills before the Legislature that have a bearing on the health and/or Medicare, and the subject of Abortions was included. Support of Fluoridation will be continued.

Clyde Deming, Chairman of the Ad Hoc Committee for the Doctor of the Year Award reported that the name of Luca E. Celentano has been sent to the office of the Connecticut State Medical Society with a story of his background.

Harvey Fritz, Chairman of the Insurance Committee reported that changes have been made in insurance coverage which must be agreed upon by the individual to become effective. While the premium has been increased, hospital coverage will be raised to \$50.00 per day and a new maximum of \$15,000. for major medical coverage. The policy is not cancellable after age 70, and members over 70 must be accepted under conditions. There is a supplemental long term disability income coverage also.

The Board of Governors passed a motion to go on record as being in favor of usual and customary

fees in contrast to a fixed schedule, and this decision has been reported to the Council, Dr. William Horton of CMS and to the Chairman of the Insurance Committee.

The Clerk reported that New Haven County Medical Association has received acknowledgement from several of the high schools in the County for the A.M.A. book entitled *Today's Health Guide* which was paid for by the association and distributed with the assistance of the Woman's Auxiliary to the thirty high schools in the County.

This was the last regular meeting of the 1968-1969 Board of Governors until after the annual county meeting on March 27, 1969 when the new Board of Governors will be elected.

A social hour and dinner followed.

Respectfully submitted

William L. West, M.D., Clerk

185th Annual Meeting

New Haven County Medical Association

March 27, 1969

The 185th Annual Meeting of the New Haven County Medical Association was held on Thursday, March 27th at Waverly Inn, Cheshire, Connecticut. The President introduced and the members heard comments from the following visitors: Officers of Connecticut State Medical Society: Norman H. Gardner, President; Stevens J. Martin, President-Elect; William R. Richards, General Manager; and Frank K. Abbot, Vice-Speaker of the House of Delegates.

Mr. Arnold Olson, Executive Secretary of Fairfield County Medical Association and Martin Friedman, Fairfield County Delegate, expressed their pleasure at attending the New Haven County Meeting and indicated that "meetings are for meeting people." Frank Lovallo brought greetings from Middlesex County and Edward Palomba was present from Tolland County.

Our Councilor, Stewart J. Petrie, commented on his report which was previously mailed to the membership. Referring to the Title XIX Problem, Dr. Petrie reported that Dr. Max Goldstein's report to the Council will be published in *Connecticut Medicine*. A Connecticut State Medical Society ad hoc committee was moved, seconded and adopted, with Dr. Goldstein as Chairman, to study and to further implement his suggestions. Associate Councilors Dr. Pelz and Dr. Granoff added to Dr. Petrie's re-

(Continued on page 338)

OBITUARIES

Frank D. Ursone, M.D.

1900-1969

Dr. Frank D. Ursone died while vacationing in Florida on March 25, 1969.

He was born in Hartford, Connecticut on October 26, 1900. He received his B.S. and M.D. degrees from



Tufts University, Boston, Massachusetts. He interned at St. Francis Hospital, Hartford, Connecticut from 1929 to 1931 and then did a year residency in radiology at Pennsylvania Hospital.

Dr. Ursone began general practice in Norfolk, Connecticut on April 10, 1933. He was a true family practitioner, giving full coverage to his patients from the cradle to the grave. They knew that they could depend on him night or day, winter or summer.

He was on the staff of the Litchfield County Hospital, Winsted, Connecticut, being senior attending in medicine with privileges in obstetrics, pediatrics, and minor surgery. He interpreted the electro-cardiograms at the hospital until he retired to the honorary staff.

Dr. Ursone was a member of the Litchfield County Medical Association, Connecticut State Medical Society, American Medical Association, Connecticut Association of General Practitioners, The American Association of General Practitioners, Connecticut Public Health Association, The American Public Health Association and The American Association for the Advancement of Science.

He belonged to many civic associations; Norfolk Volunteer Fire Department, Rotary, Benevolent Or-

der of Elks, Knights of Columbus, Old Newgate Coon Club, and the Canaan Amateur Radio Club.

His hobbies were astronomy, mineralogy, and amateur radio.

He was director of health and medical examiner for the Town of Norfolk.

Dr. Ursone leaves his wife, two sons, two daughters, and several grandchildren.

Francis Gallo, M.D.

William J. Watson, M.D.

1907-1969

Dr. William J. Watson, 62, of 80 Elbridge Road, New Britain, Connecticut, died suddenly on March 5, 1969.

Since 1933 when he started to practice as a family doctor, Dr. Watson has been a leader in the medical



community. He early recognized the trend toward specialization and, with considerable personal sacrifice, qualified himself as a specialist in general surgery.

He served with distinction in World War II as a lieutenant commander in the United States Navy, subsequently became a diplomate of the American Board of Surgery and returned as a senior attending surgeon to New Britain General Hospital, where his contributions have been notable.

His broad range of activities were manifested among other things by his interest in the law, which culminated in a law degree obtained while carrying on a busy practice. He was immediately admitted to

the Connecticut State Bar and became New Britain's first lawyer-physician.

Most recently Dr. Watson relinquished his practice to organize the full time emergency room coverage at the New Britain General Hospital, where he became chief of the department.

Dr. Watson was a member of the New Britain Medical Society, Hartford County Medical Society, Connecticut State Medical Society, and the American Medical Society. He was also a Fellow of American College of Surgeons and a member of the American Board of Surgery, and a communicant of St. Maurice Church.

Surviving are his wife, Marie Coburn Watson; three sons, James J., William J. Jr., and Robert E., and a daughter, Miss Jane Watson, all of New Britain.

Harold M. Clarke, M.D.

In Memoriam

Crandall, Bradford B., Mystic, Wisconsin 1934. Dr. Crandall was a general practitioner in the Groton area for over 20 years. He served as a Navy officer in World War II. He came to the Submarine Base as executive officer of the medical unit in 1945 but left active duty in 1947 to become a commander in the Navy Reserve. Dr. Crandall retired from the Navy Reserve in 1968 with the rank of Captain. Dr. Crandall was recently appointed a medical examiner for New London County. He was a staff member of Lawrence Memorial Hospital, Westerly hospitals and house physician of the Old Mystic Nursing Home. He was a member of the Connecticut Academy of General Practice, the New London County Medical Association and the Connecticut State Medical Society. Dr. Crandall died March 13 at the age of 61.

Ives, Eli B., Bridgeport, Tufts 1912. Dr. Ives was a general practitioner in the Bridgeport area for many years. He was a senior physician at Bridgeport Hospital and on the courtsey staff at St. Vincent's Hospital. Dr. Ives was a member of the American Academy of General Practice, the Connecticut State Medical Society and the American Medical Association. Dr. Ives died March 15 at the age of 56.

Loiacono, Anthony J., New London, Harvard 1927. Dr. Loiacono was a surgeon in the New London area. He was Fellow of the American College of Surgeons, and the Connecticut State Medical

Society. Dr. Loiacono died December 20, 1968 at the age of 68.

Saposnik, Jacob J., West Haven, Harvard 1933. Dr. Saposnik was a general practitioner in the West Haven area. He was a member of the Connecticut State Medical Society. Dr. Saposnik died on March 17 at the age of 62.

New Haven County Medical Association 185th Annual Meeting

(Continued from page 336)

port. Dr. Pelz will submit an article to *Connecticut Medicine* dealing with the County Review Committee.

The Clerk, Hyman A. Levin, reported the financial status of the association and submitted a membership report for the year as follows:

Membership, January 1, 1968	1,029
New members added	46
	<hr/>
	1,075
Members Lost	47
	<hr/>
Membership, December 31, 1968	1,028

Dr. Levin also spoke of the record of the late Max Caplan in terms of service to our county, state and national organizations, saying "his untimely passing denied him the presidency of the State Society and further honors in the A.M.A."

Luca Celentano, Chairman of the By-Laws Revision Committee, presented proposed amendments to the By-Laws. These were placed on the table for consideration at the semi-annual meeting in October.

Bernard Burnham, Chairman of the State Legislation Committee, reported a long list of bills which are up for action by the Legislature. Of particular interest was one dealing with payment to physicians by the Welfare Department.

At the Annual Meeting, a total of 16 candidates were elected to Provisory membership. Also, 30 Delegates for a two year term and 30 Alternate Delegates for a one year term were elected. The new officers elected for 1969-1970 are:

President, Kurt Pelz, Wallingford; Vice-President, Stewart J. Petrie, Derby; Clerk, William L. West, Derby; Member, Executive Committee, Charles C. Verstandig, New Haven.

Beginning their second year of their 1968-1970 terms are:

Councilor, Stewart J. Petrie, Derby; Associate Councilor, Kurt Pelz, Wallingford and Associate Councilor, Morris A. Granoff, New Haven.

Morris Granoff, New Haven, proposed Amendments to the By-Laws which dealt with Nominating Committee procedure. These were then placed on the table. He also stressed the lack of interest in Compac by the members and made suggestions to implement the political education of members.

Leonard Parente, Health Officer of Hamden, was named chairman of an ad hoc committee to Study the Phelps Community Project.

Following adjournment, there was a social hour, and then the 17th Joint Dinner with the members of the woman's Auxiliary. A total of 238 dinners were served. During the dinner door prizes were awarded to the holders of lucky tickets. A plaque was presented to Charles Verstandig, the retiring President by Jacques Green, and Dr. Verstandig responded with closing remarks.

Respectfully submitted,

WILLIAM L. WEST, M.D., Clerk

ACTH Versus Corticosteroids

The package inserts accompanying corticotropin (ACTH) preparation (Acthar; and other brands) recommend the use of ACTH for many disorders. ACTH can be useful in steroid-responsive conditions, but oral corticosteroids can achieve the same therapeutic goals, usually more predictably, more conveniently, less painfully, and at less cost.

ACTH is uniquely useful as a diagnostic tool for determining the competence of the pituitary-adrenocortical axis. The Thorn test—response of the peripheral eosinophil count to ACTH administration—is cited in one insert as a measure of adrenal responsiveness; this test was long ago superseded by direct measurement of plasma or urine 17-hydroxycorticosteroids after administration of ACTH.

ACTH IN ADRENAL SUPPRESSION—the degree of suppression of the hypothalamo-pituitary-adrenal axis caused by the administration of corticosteroids is related to dose and duration of therapy. Although suppression may be prolonged, it is rarely irreversible. When therapy is stopped, corticosteroid levels often return to normal within a month, though the response to stress (such as insulin-induced hypoglycemia) may not be adequate for as long as a year (T. Livanou et al., *Lancet*, 2:856, 1967).

In a study of 14 patients with marked pituitary-adrenal suppression due either to adrenocortical

tumors or to prolonged corticosteroid therapy, A. L. Graber et al. (*J. Clin. Endocr.*, 25:11, 1965) found that recovery of the adrenal itself (measured by plasma 17-hydroxycorticosteroids) was preceded by recovery of the pituitary (measured by plasma ACTH levels). If correction of pituitary function is necessary before adrenal recovery can occur, the rationale for the use of ACTH to stimulate the adrenal cortex during corticosteroid withdrawal is unclear; exogenous ACTH at this time may prolong suppression of endogenous ACTH production by the pituitary and thus delay adrenal recovery.

After seven-to ten-day courses of therapy, corticosteroids can usually be withdrawn abruptly without fear of precipitating adrenal crisis. After prolonged corticosteroid administration, however, dosage should be gradually reduced over a month or more, with titration of the rate of withdrawal against exacerbation of symptoms of the illness for which the steroids were prescribed. The administration of corticosteroids on alternate days (J. G. Harter et al., *New Eng. J. Med.*, 269:591, 1963) or for three consecutive days each week (D. A. Adams et al., *Ann. Intern. Med.*, 64:542, 1966) has been reported to produce less adrenal suppression than a daily-dose regimen, with correspondingly less hazard on withdrawal. During the period of recovery from adrenal suppression, surgery or other stress can precipitate adrenal crisis; when adrenal crisis does develop, it is an indication for the use of corticosteroids, not ACTH.

OTHER USES FOR ACTH—Massive doses of ACTH have been reported to be effective in the control of severe refractory myasthenia gravis (K. E. Osserman and G. Genkins, *JAMA*, 198:699, 1966). Hospitalization is mandatory for such therapy since remissions is preceded by an exacerbation of symptoms that may require the facilities of a respiratory-care unit.

M. Friedman and L. B. Strang (*Lancet*, 2:568, 1966) reported that CATH therapy in children does not inhibit growth to the same extent as corticosteroid therapy, if at all. If their data are confirmed, ACTH may replace corticosteroids in the treatment of some children with chronic diseases responsive to long-term steroid therapy. There is some belief that ACTH has special value in the treatment of ulcerative colitis, but the belief has not yet been put to the test of an adequately controlled trial.

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y. Vol. 10, No. 16.

MEETINGS

GENERAL

May 13, 14, 15

177th Annual Meeting, Connecticut State Medical Society

Hartford Hilton Hotel

July 13-17

118th Annual Convention, American Medical Association

New York City

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospital, New London

May 6 7:15 P.M.

The Peripheral Nerve and Neuromuscular Function and their Disorders; The Physiology and Anatomy of Epilepsy.

H. Richard Tyler, M.D., Assistant Professor of Neurology, Harvard Medical School.

May 20 7:15 P.M.

Parathormone—Thyrocalcitonin

Dorothea Hellman, M.D., Assistant Professor in Medicine and Pediatrics, Tufts Medical School

MEDICINE

Wednesdays 12:00 P.M.-1:15 P.M.

Pulmonary Diseases and Pulmonary Physiology

Radiation Center Conference, Room, Hospital of St. Raphael, New Haven

Chairman: John B. Berte, M.D., Director, Department of Pulmonary Diseases and Inhalation Therapy, Hospital of St. Raphael

Open to all physicians

Thursdays 1:30 P.M.-3:30 P.M.

Hematology

Hematology Laboratory and Wards, Hospital of St. Raphael, New Haven

Robert P. Zanes, Jr., M.D., Hospital of St. Raphael

Open to all physicians

May 15-17

Fifth Annual Cardiovascular Symposium

St. Francis Hospital, Hartford

Program: Advances in the Diagnosis and Treatment of Arrhythmias, Howard B. Burchell, M.D., Editor, "Circulation," Professor of Medicine, University of Minnesota Medical School; Present Status of Valvular Homografts and Heterografts, James R. Malm, M.D., Associate Professor of Surgery, Columbia University College of Physicians and Surgeons; Pathology of Coronary Artery

Disease and Its Complications, Jesse E. Edwards, M.D., Clinical Professor of Pathology, University of Minnesota Medical School; Secrets in the Shadows—A Clinician's View of Cardiovascular Radiology, Joseph K. Perloff, M.D., Associate Professor of Medicine, Georgetown University; Cardiac Auscultation in Acquired Heart Disease, Bernard L. Segal, M.D., Clinical Associate Professor of Medicine, Hahneman Medical College; Acute Pericarditis, David H. Spodick, M.D., Assistant Professor of Medicine Tufts University Medical School; Viral Diseases of the Values and Heart, Papillary Muscle Syndrome, George E. Burch, M.D., Editor, American Heart Journal, Professor and Chairman, Department of Medicine, Tulane University Medical School, Surgical Indications in Congenital Heart Disease, Alexander S. Nadas, M.D., Clinical Professor of Pediatrics, Harvard Medical School.

May 24

Eighth Annual Advanced Contact Lens Seminar

Postgraduate Institute of the New York Eye and Ear Infirmary

Discussion: Soft lenses and aphakia; methods of fitting keratoconus, corneal grafts, astigmats and children

Fee: \$75 (luncheon and cocktail reception included). For registration write to Jane Stark, Registrar, 310 East 14th Street, New York City

PEDIATRICS

May 21

Scientific session sponsored by the New England Pediatric Society and New Haven Area Rehabilitation Center

Speakers: Yale Medical School, Viral Infections in Pregnancy as a Cause of Fetal Damage, Dorothy Horstman, M.D., Professor of Epidemiology and Pediatrics; The Effects of Maternal Analgesic Agents on the Fetal Heart Rate, Edward Hon, M.D., Associate Professor Obstetrics and Gynecology; Recognition of Minimal Brain Damage in Early Infancy, Sally Provence, M.D., Professor of Pediatrics; Minimal Brain Damage—Conceptions and Misconceptions, Ethelyn Klatskin, M.D., Assistant Professor Of Psychology; Behavior of the 'Brain Damaged' Child; John Schwalter, M.D., Assistant Professor of Pediatrics and Psychiatry. Early Educational needs of the Deaf Child, David Green.

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NEW BOOKS IN REVIEW

HANDBOOK OF PEDIATRIC MEDICAL EMERGENCIES. 4th Edition. Edited by Charles Varga, M.D. and Contributors. The C. V. Mosby Company, St. Louis, 1968. 694 pp. with 120 illustrations. \$19.75.

Reviewed by: LOUIS H. NAHUM

The basic principles in dealing with medical emergencies in this edition have not been altered. However, there are present some recent changes suggested for emergency care. Ten of the chapters have been entirely rewritten by new contributors to this edition. One on pediatric inhalation therapy which has frequently been employed and clarity and orderliness is characteristic of it throughout. The chapter on pediatric procedures has been extensively rewritten and illustrated beautifully especially the equipment useful in the care of the newborn.

Several changes have been made in the sections devoted to the management of poisonings and helpful is the alphabetical arrangement in place of previous separation of poisonings due to drugs or to agents in household chemicals. The physician who has need to determine the poisonous ingredients in any commercial preparation can use the index to find the page on which treatment is outlined. In addition all toxic agents referred to in the reference pages 610-614 are italicized.

The essence of scholarship is often displayed in the quotes an author uses to introduce an idea or in this case a chapter for "next to the originator of a good sentence is the first quoter of it" as we are told by Ralph Waldo Emerson. And so we find each of the eighteen chapters perfectly introduced by well chosen apt quotations.

The introduction by Professor Varga is a scholarly overview of every viewpoint involved in understanding the problem of emergencies; from the viewpoint of parent, patient, physician, hospital, school authorities and from viewpoint of human morality. It is perfectly conceived with an attempt to introduce logical thinking via computerized programming.

A concluding quote from the late Dr. J. Coleman Edwards gives the motif to this excellently produced volume "The success of the future generation lies dormant in this child. Therefore in this hour the future of tomorrow lies in your hands. How then will you shape his destiny and that of the world? Yours is an awesome responsibility. Fulfill that responsibility as if your very life depended upon it!" If physicians follow this handbook they will succeed in fulfilling their responsibility.

ALCOHOL AND THE IMPAIRED DRIVER: A MANUAL ON THE MEDICOLEGAL ASPECTS OF CHEMICAL TESTS FOR INTOXICATION. American Medical Association, 1968. 234 pages, 10 chapters, 11 tables, and 21 figures. Price not specified.

Reviewed by: LOUIS H. NAHUM

Measurements of blood-alcohol levels in this book are stated in terms of percentage weight by volume based on the number of milligrams of alcohol per 100 milliliters of blood to eliminate ambiguous legal interpretations.

The first chapter is devoted to alcohol and traffic safety and is concerned with characteristics of the drinking driver, public attitudes towards the drinking driver, chronic medical

conditions and traffic accidents. The next three chapters are devoted to toxicology of alcohol. Then an important chapter on effect of alcohol on driving ability, one on chemical tests for determination of ethyl alcohol. Chapter 7 is devoted to measures for control of drinking drivers. Chapter 8 is on medicolegal aspects of alcohol and traffic safety. An important chapter is 9 on constitutional aspects of chemical-test evidence. The last chapter is devoted to medicolegal aspects of chemical tests. The book is made complete by an appendix presenting a model program for the control of alcohol for traffic safety. Finally there is an extensive bibliography of scientific references.

The book is perfect for the subject and is a must for physicians and lawyers. For there is probably no more authoritative treatment of the medical and legal aspects of alcohol anywhere to be found.

SYNOPSIS OF GYNECOLOGY. 7th Edition. Edited by Daniel Winston Beacham, M.D. and Woodard Davis Beacham, M.D. The C. V. Mosby Company, St. Louis, Missouri, 1967. 105 figures and 1 color plate, 384 pp. \$8.50.

Reviewed by: C. LEE BUNTON

This pocket edition textbook of Gynecology amply fulfills the purpose for which it was written—i.e. to provide a synopsis for the medical student who must know something about speciality subjects but who is not necessarily going to concentrate in this area of the practice of medicine. The authors also suggest in the preface to the 7th edition that it might be convenient as a brief reference work for the general practitioner or other specialists who wish to find some superficial information concerning gynecology.

Various aspects of this speciality, even including those of medical legal problems, are covered with surprising completeness for such a brief volume. This is accomplished by being necessarily pedantic about diagnostic features and diagnostic techniques, the pros and cons of which would be more fully discussed in a larger volume. For instance, in the section on infertility investigations it is suggested that an endometrial biopsy be taken "at the onset of menstruation", whereas many would suggest that it would be more advisable to take the biopsy during the latter part of the menstrual cycle. On the other hand, several varieties of pregnancy tests are discussed, bio-assays being described along with immunological techniques, which seems hardly necessary in this type of textbook.

The style of writing is easy to read, sometimes colloquial (a contraceptive diaphragm is called a "gadget") and certainly straightforward.

Appropriate illustrations, some in color, as well as excellent drawings enhance the text throughout. The sections on anatomy, physiology and gynecological examination comprise more than a third of the book which seems especially appropriate considering the use for which it is intended.

Although not expensive as textbooks go (the price is \$8.50) possibly a paperback edition might make it easier for the medical student to own a copy to say nothing of greater ease in carrying it around in his pocket.

DECISION MAKING IN NATIONAL SCIENCE POLICY. *A Ciba Foundation Symposium. Edited by Anthony De Reuck, Maurice Goldsmith and Julie Knight. Little, Brown & Company, Boston, 1968. 310 pp. Illustrated. \$12.00.*

Reviewed by: JOSEPH S. FRUTON

Since World War II, the increase in government expenditure for scientific research and for the application of scientific knowledge in medicine and technology has inevitably forced national leaders to recognize the necessity of making sounder choices among various scientific objectives, and has obliged "pure" scientists to consider the relevance of their work to social needs. This relatively recent efflorescence of interest in the social function of science is an acknowledgement of the correctness of much maligned views expressed in the 1930's by a few scientists, notably J. D. Bernal. The volume under review is a useful addition to the burgeoning literature on this subject.

The book contains the papers presented at a symposium held in April 1967 at the Ciba Foundation in London, and includes the informal discussion among the participants. The introductory papers by Lord Todd (the chairman), Sir Solly Zuckerman, and A. M. Weinberg were followed by groups of talks under the general heading of 1) evaluation of research productivity; 2) science policy in mixed economies (France, Sweden, United States, Canada); 3) science policy in planned economies (Soviet Union, Hungary); 4) science policy in developing countries (Argentina, India, Israel).

The variety of approaches and opinions evident in the symposium make it impossible to summarize adequately the contents of the book. The central question to which most of the 28 participants addressed themselves was whether a rational basis can be developed for making national decisions affecting science. Some speakers (notably R. L. Ackoff) defended the view that operational research can provide "scientific" criteria of choice, but the prevailing opinion (best expressed by Todd) was that the basic elements in national decisions affecting science are political in nature. The clearest documentation of this position was provided by W. D. Carey (Assistant Director, U.S. Bureau of the Budget).

At a time when American scientists must adjust to the plateauing of government support for their research, discussions such as this one are a valuable corrective to the smug assumption that the scientific enterprise needs no justification in terms of its appeal to political leaders. For the concerned reader, whatever his bias may be, the opinions expressed in the symposium may be a useful guide to the kinds of justifications needed to produce the desired political response.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

Todd-Sanford Clinical Diagnosis By Laboratory Methods. 14th Edition. Edited by Israel Davidsohn, M.D. and John Bernard Henry, M.D. W. B. Saunders Company, Philadelphia, 1969. 1308 pp. with 698 illustrations. \$24.00.

Current Therapy, 1969. Edited by Howard F. Conn, M.D. W. B. Saunders Company, Philadelphia, London and Toronto. 945 pp. \$15.00.

Collateral Circulation In Clinical Surgery. Edited by D. E. Strandness, Jr., M.D. W. B. Saunders Company, Philadelphia, London, Toronto, 1969. 633 pp. with 242 illustrations. \$18.50.

Physiology of the gastrointestinal tract. Edited by E. Clinton Texter, Jr., M.D., Ching-Chung Chou, M.D., Higinio C. Laureta, M.D. and Gaston R. Vantrappen, M.D. The C. V. Mosby Company, St. Louis, 1968. 262 pp. with 106 illustrations. \$10.75.

Renal disease in childhood. Edited by John A. James. The C. V. Mosby Company, St. Louis, 1968. 371 pp. with 104 illustrations. \$18.50.

Water and electrolyte metabolism and acid-base balance. Edited by Edward Muntwyler, Ph.D. The C. V. Mosby Company, St. Louis, 1968. 169 pp. with 33 figures. \$5.85.

Dr. Wilbur Accepts Editorship

Dwight L. Wilbur, M.D. will become editor-in-chief of *Postgraduate Medicine* following completion of his term of office as president of the American Medical Association. He will be succeeded as AMA president by Gerald D. Dorman, M.D., during the AMA Annual Convention July 13-17 in New York City.

Postgraduate Medicine, a McGraw-Hill publication, is published monthly in Minneapolis, Minn., with a paid circulation of 51,000. It contains original articles on applied medicine.

Dr. Wilbur previously served for 21 years as editor of *California Medicine*, official Journal of the California Medical Assn., and as chairman of the editorial board of the *Journal Gastroenterology*. He has been a member of the editorial board of *Postgraduate Medicine* since 1951.

As editor-in-chief, Dr. Wilbur will succeed the late Charles W. Mayo, M.D., who held the position from the time the publication was founded in 1947 until his death in 1968.

Connecticut Medicine

MANUSCRIPTS

Manuscripts, including references or bibliography, must be typewritten, double-spaced on white paper 8½ x 11 inches with adequate margins on firm paper. The original copy, not the carbon copy should be submitted. Carbon copies or single spaced manuscripts will not be considered. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Receipt of manuscripts will be acknowledged and unused manuscripts returned. *Accepted* manuscripts become the permanent property of the JOURNAL and may not be reprinted elsewhere without permission from both the author and CONNECTICUT MEDICINE. The author is responsible for all statements made in his work, including changes made by the copy editor.

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the JOURNAL (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration as well as typed on a separate sheet. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. CONNECTICUT MEDICINE will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also marked copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

ADVERTISING

All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by CONNECTICUT MEDICINE.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

REPRINTS

Reprint orders should be returned at once as the type will be destroyed immediately following publication of the manuscript. The JOURNAL does not stock reprints of the articles published. Requests for individual reprints should be sent to the author.

Communications should be addressed to CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Conn., 06511 Telephone 865-0587.

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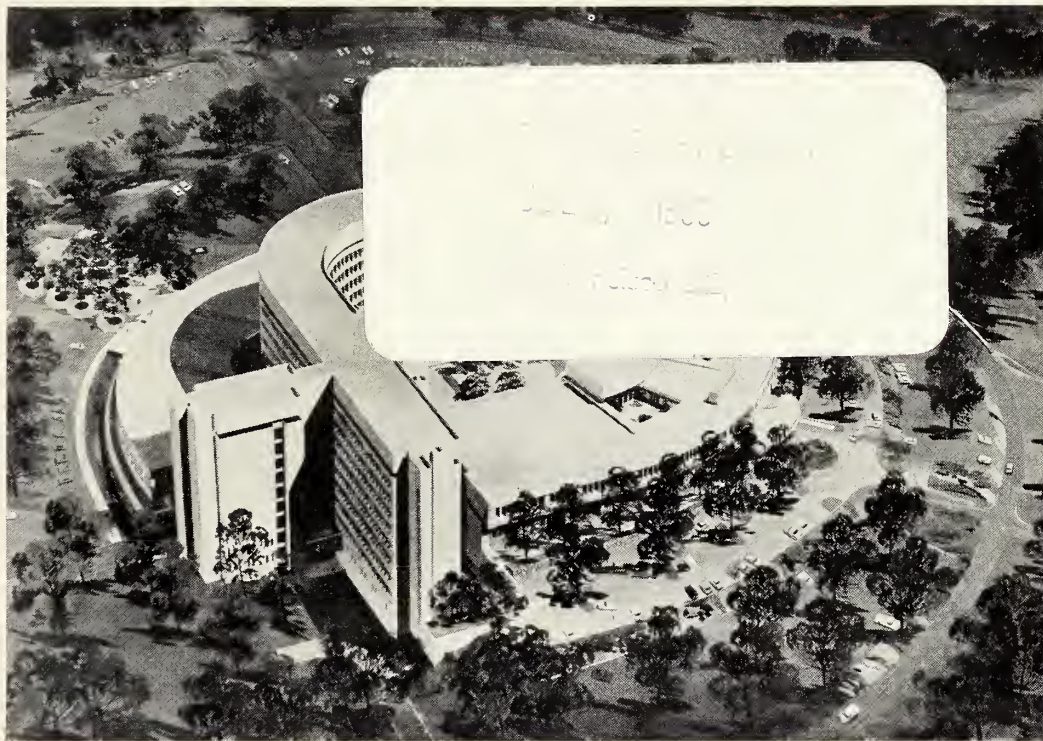


Connecticut Medicine

Connecticut State
Medical Journal

Volume 33/June 1969/Number 6

John W. Patterson, M.D., Dean, Guest Editor



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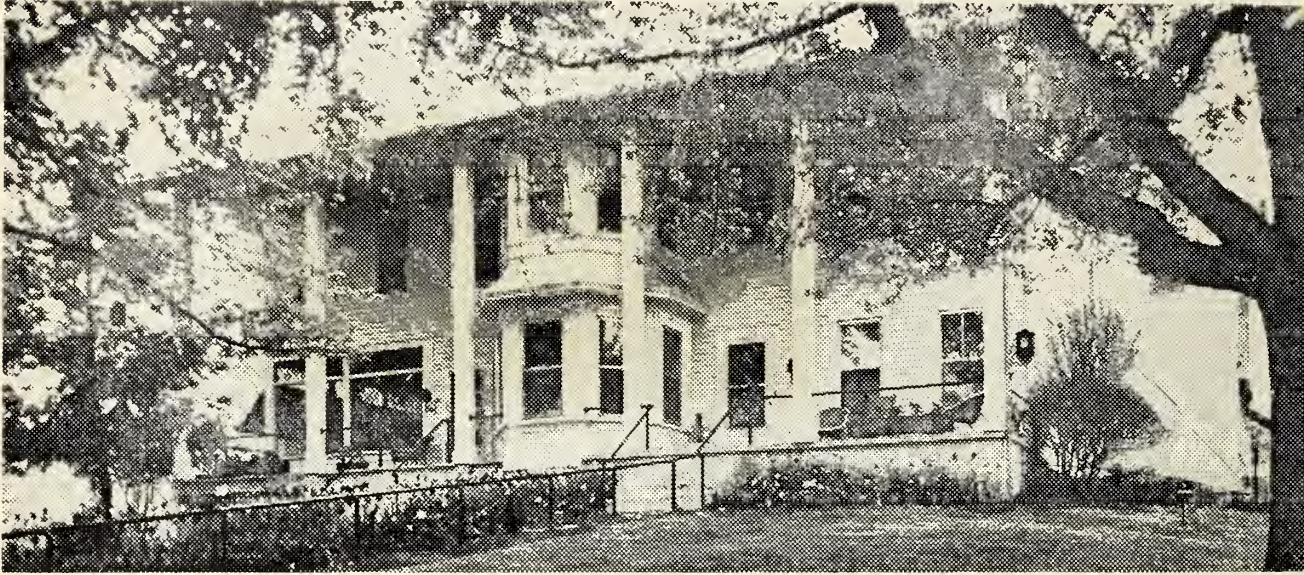
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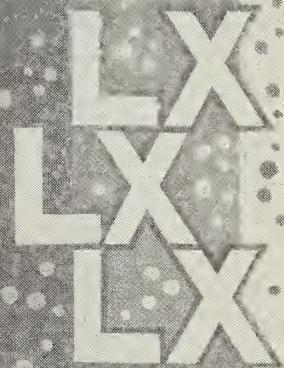


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References:

- (1) Siver, R. H.: CMD, 21:109, September 1954.
- (2) Frykman, H. H.: Minn. Med., 48:19-27, January 1955.
- (3) McGivney, J.: Tex. State Jour. Med., 51:16-18, January 1955.
- (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., 15:15-16, October 1965.
- (5) Weekes, D. J.: N.Y. State Jour. Med., 58:2672-2673, August 1958.
- (6) Weekes, D. J.: EENT Digest, 25:47-59, December 1963.
- (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961.
- (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., 20:591-593, November 1965.



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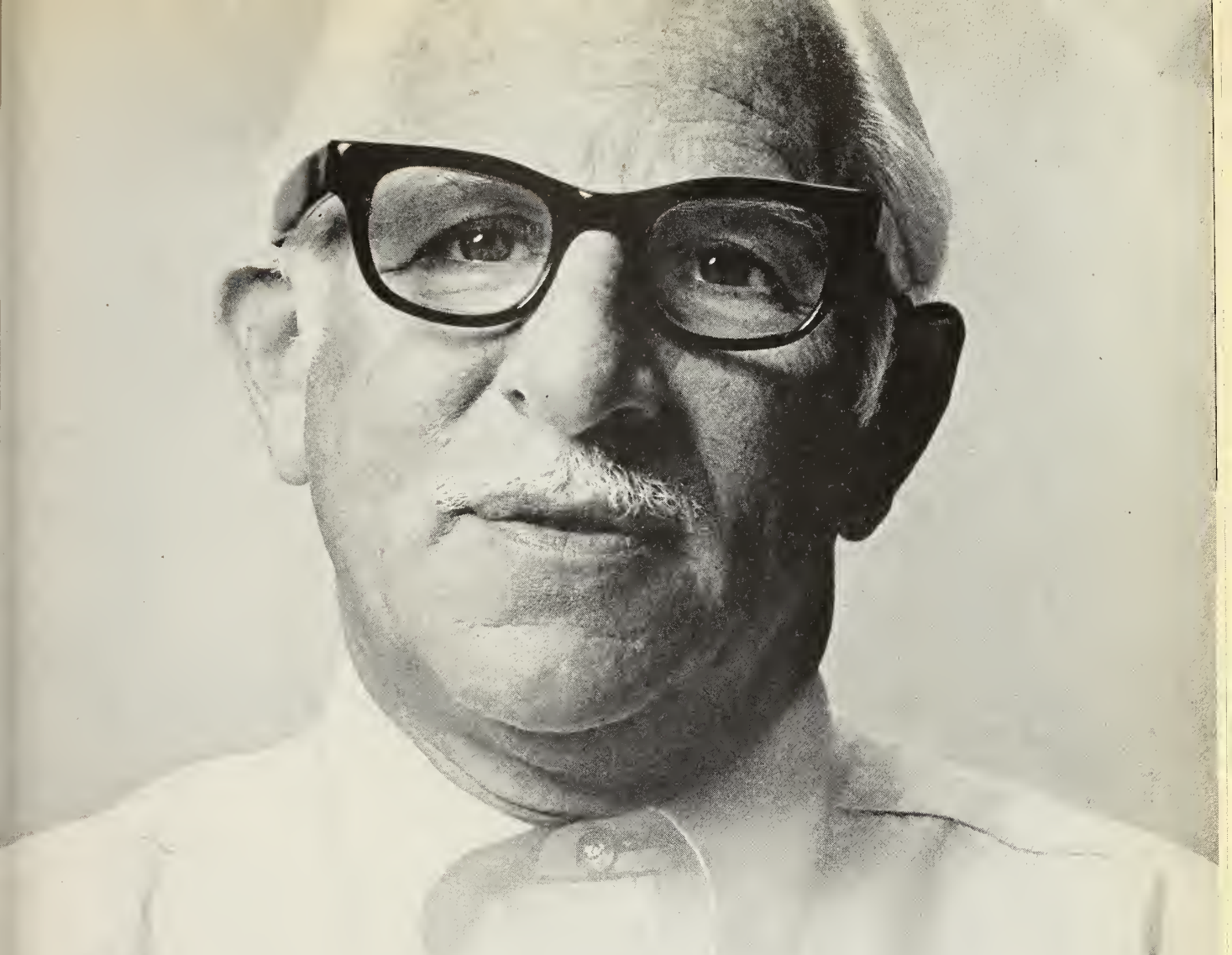
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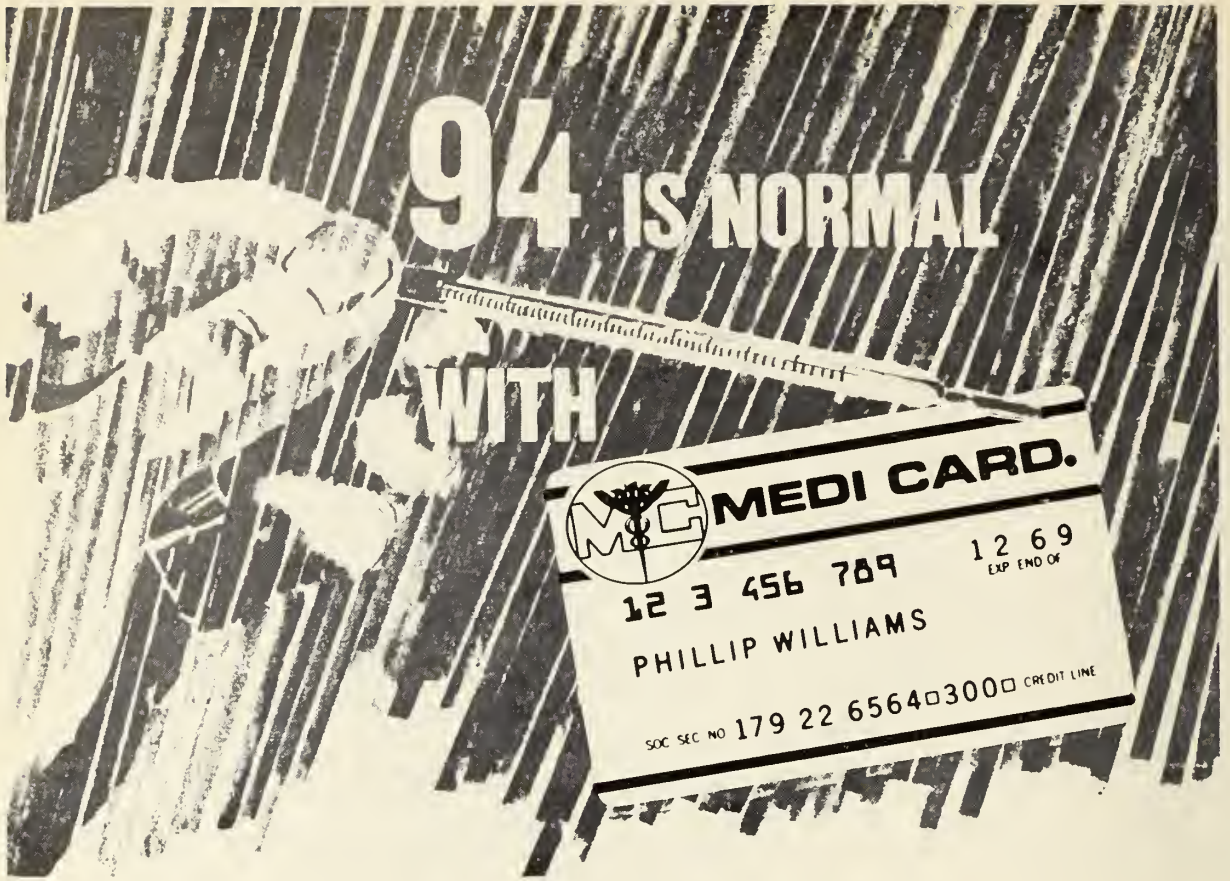
stant observation is essential. If new infections appear, appropriate measures should be taken.

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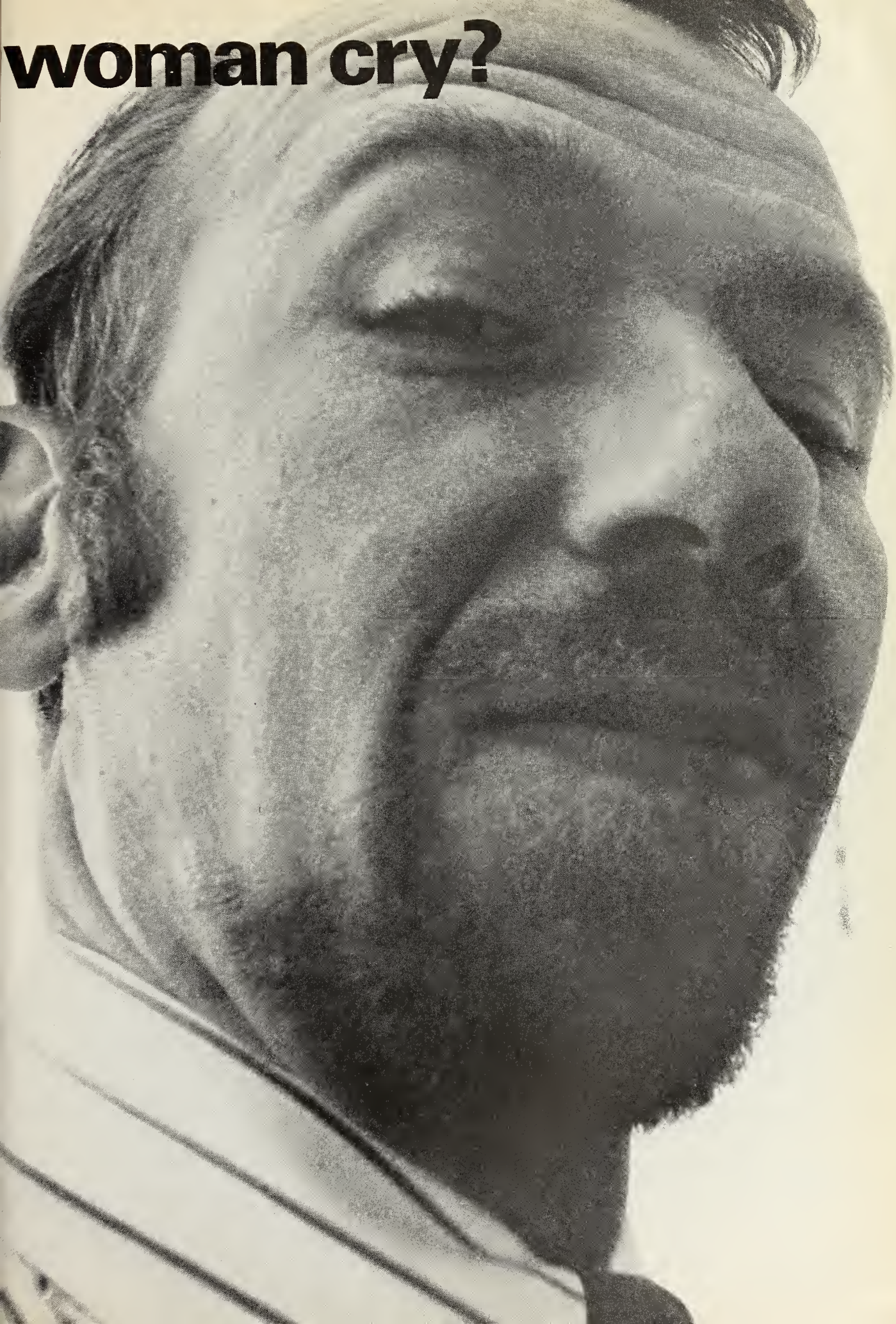
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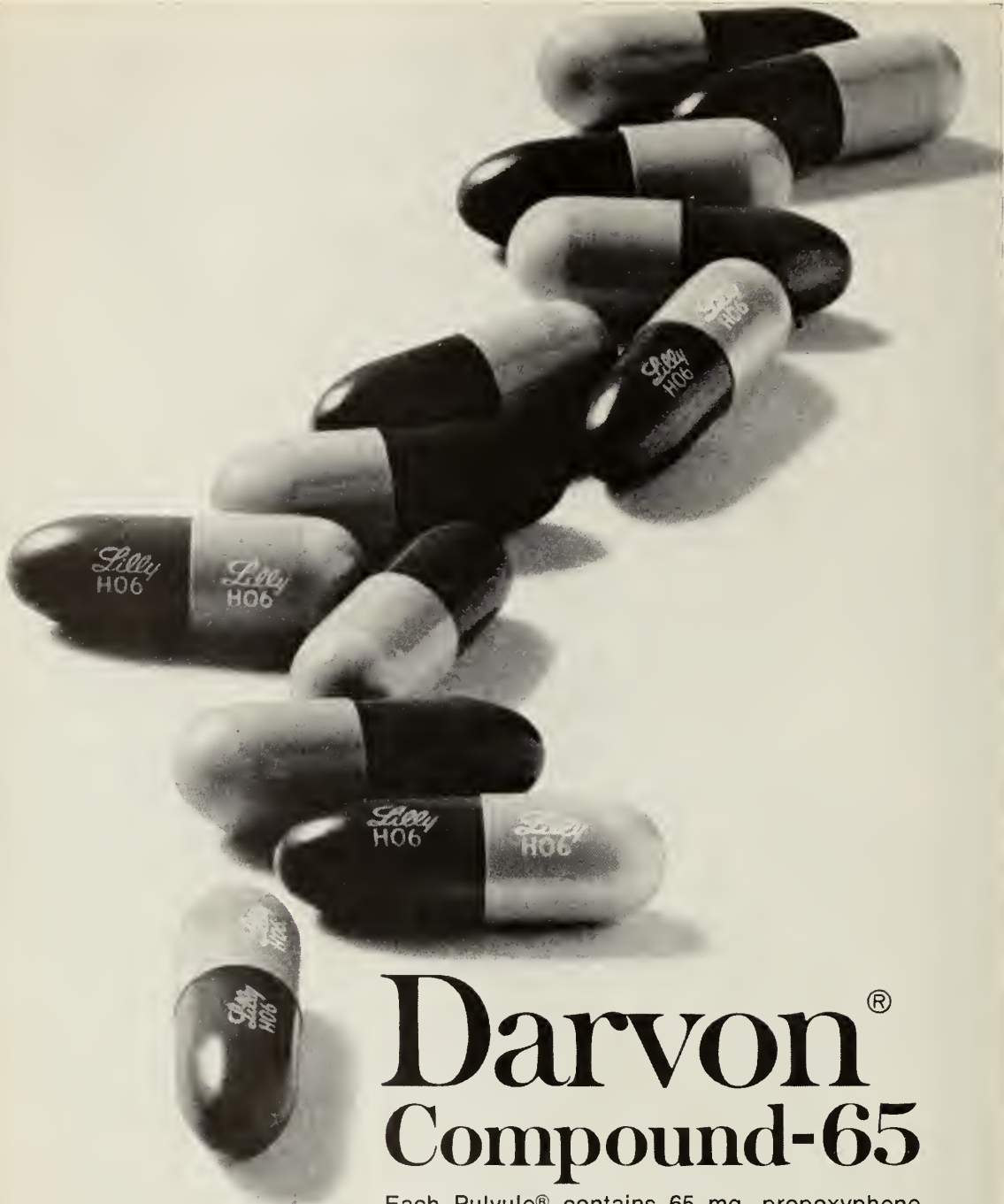
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Connecticut Medicine

editorials

Studies In Human Ecology: Fetal Death Rate In Relation To Atomic Bomb Testing

It is an established fact that the fetus and infant are highly sensitive to radiation and the effect of X-rays. This has been determined in studies on both animals and man. Apparently this sensitivity results from the rapid cell division and organ formation characteristic of early phases of development. It is therefore to be expected on theoretical grounds that the first serious effect of fallout from bomb explosions would appear in the fetus and young infant for which existing measurements show very much higher organ and skeletal doses than for the adult.

The question arises how strontium 90 in fallout, aside from concentrating in the bone also appears to produce genetic damage which expresses itself in excess of fetal death when injected in the male parent animal prior to reproduction. Sternglass¹ points out that the doubling dose for chromosomal damage to human cells may be as low as 1 rad. This is consistent with recent evidence for an increase in childhood leukemia many years after the irradiation of either parent at diagnostic X-ray levels. Such findings suggest that both the excess fetal and infant deaths are primarily due to chromosomal damage produced just prior to conception or in the earliest phases of development.

If this is so there should be an association between infant mortality and fallout after atomic bomb explosions. Sternglass documents clearly that even relatively low level doses from peace time fallout lead to detectable increases in death rates especially for the sensitive embryo fetus and infant. This was first observed in fetal death rates in the Albany-Troy area following the rain out of radioactive debris from a 43 kiloton test in Nevada in 1953. The increase in fetal deaths was followed also by an increase in childhood leukemia beginning some five years later. Both of these observations appeared to suggest a causal connection between the increase in fetal deaths and the arrival of the fallout.

This raised the question whether changes in fetal deaths appeared not only in the Albany-Troy area but also in New York State as a whole and whether subsequent tests are also reflected in increases in fetal mortality. Sure enough the same phenomenon was observed in the whole of New York State. Fetal mortality was declining in 1935-1950 only to begin to increase reaching 23 per 1000 live births between 1957-1963. In 1964 it increased sharply to 27.3 per thousand. A similar phenomenon was observed in California after the hydrogen bomb tests in the Pacific in 1954.

The question was whether there was a connection between rise in fetal mortality over the expected rate and the accumulated fallout of Sr. 90 deposited

THE COVER

The cover picture shows the University of Connecticut Health Center complex which is being constructed in Farmington. The high-rise "L" shaped structure provides space for faculty offices and laboratories on the upper seven floors. The library and other administrative activities are located in the lower floors. Hospital nursing units are arranged one above the other in the two somewhat circular shaped high-rise wings. Only one of these will be built initially. The outpatient clinics are located in the lower fan shaped structure towards the front of the picture. A similar low-rise fan shaped structure behind the high-rise portion houses the student lecture rooms and laboratories. The square shaped high-rise wing at the opposite end from the patient care units provides a facility for animal care.

in the New York area, and there was. There was a decrease in fetal deaths coincident with temporary stoppage of nuclear testing in 1958-1961 and a sharp rise in fetal mortality beginning with the large USSR test series in 1961.

A similar pattern in the registered fetal death rate and the rate of stillbirths exist in the data for the United States as a whole for all periods of gestation up to nine months. The same pattern of increased infant mortality up to one year of age exists in association with nuclear weapons testing but differs in various states according to precipitation and therefore fallout accumulation. The "wet" states show increased mortality of fetus and infant, the "dry" states less so.

Apparently there is no natural plateau of 20-25 per 1,000 live births because in six European countries with advanced medical care, the infant mortality continued down and fell below that of the United States in 1961. The lowest level for that of Sweden reached 14.2 in 1964 when the United States rate was still 24.8 per 1,000 live births. Such a rate represents an excess of 75 per cent relative to that for Sweden and an excess of 60 per cent relative to the expected United States rate of 15.5 had the infant mortality continued to decline at the 1935-1950 rate of decrease when the decline closely paralleled that for Sweden.

Public health organizations have made a world-wide effort to understand the origin of the increase in infant mortality as compared to that of other countries of equally low mortality and only the fallout from atomic explosions seems to explain the disturbing trend which has by now started to affect the entire world. Some people have asked why with improvement on medical care during the 1950's and 1960's infant mortality rates did not keep pace. The evidence clearly suggests a correlation between excesses of infant mortality and nuclear testing.

Clearly the human ova, sperm and fetus may be considerably more sensitive to internal radiation from certain isotopes than had been expected on the basis of animal experiments or observation on children irradiated in the course of diagnostic X-ray examination of the mother prior to or during pregnancy. The estimated number of excess infant deaths since 1951 alone reached 375,000 by 1966 in the United States alone and has continued at a steady rate of 34,000 per year. This despite a gradual decline of the death rate beginning with the test ban in 1963. If we calculate the life years lost from this source alone it is greater than the life years lost from all of heart disease.

The serious dimensions of the world-wide infant mortality problem are thus apparent. They suggest a need for a major international effort to test in detail the various consequences implied by the hypothesis that nuclear fallout may have played a significant role in this and other important changes in the mortality trends all over the globe. In view of the evidence of an association between nuclear testing and the increase of fetal and infant mortality in the United States an association which appears to be of a direct causal nature, the need to end all further atmospheric weapons testing and to halt all shallow underground cratering tests that permit escape of radioactive material into the environment, is of paramount urgency.

The significant increase of fetal and infant mortality seem to have been produced as the result of tests in 1945-1954 involving only a handful of kiloton weapons which are now classified as "tactical" in size. It is not difficult to imagine the full dimensions of the threat to the biological survival of mankind posed by a possible nuclear war with hydrogen bombs.

Recently the army inadvertently loosed a nerve gas into the atmosphere in Utah killing 6,000 sheep for which the army paid the owners. What would happen if the parents of fetal and infants killed by fallout banded together demanding compensation for these deaths from the United States Government.

L.H.N.

References

1. Stenglass, E. J.: Infant mortality and nuclear tests. *Bull. Atomic Scientists*, 25: 18, April 1969.

Luning, K. G.: quoted by Stenglass.

Studies In Human Ecology: The Brandywine And The Potomac

The Institute of Environmental Studies (IES) of the University of Pennsylvania was seeking an area for a long term pilot study of planned regional development. They chose for their study the basin through which the upper East Branch of Brandywine Creek runs. This area not far from Philadelphia has remained virtually uncontaminated since the Revolutionary War. However, this pastoral valley is now within easy commuting distance from downtown Philadelphia and unless something is done urbanization seems imminent. To accommodate development of this region without sacrificing scenic beauty and water quality, the IES after three years of study came up with a plan for the

river basin which is being widely acclaimed in regional planning circles.¹

Support for the study was obtained from Chester County Water Resources Authority (WRA) and funds became available from the County Commissioners and the Ford Foundation, later augmented by America the Beautiful Fund, Pennsylvania Department of Forests and Water, Pennsylvania Department of Higher Education, U. S. Geological Survey and the Federal Water Pollution Control Administration. The expertness of the project may be gleaned from the use of consultants in hydrology, limnology, sanitary engineering, landscape architecture, lawyers, appraisers, and resource planners. The cost of producing the plan was estimated at one-half million dollars.²

The goals were: 1. preservation of water supply and quality, 2. preservation of natural amenities for the enjoyment of future populations, 3. accommodation of normal growth of the region. The result was "The Plan and the Program for the Brandywine."¹ It "seemed" to have achieved all its stated goals. It treats skillfully every technical aspect of the problem except the human dimension. Water quality and natural amenity were to be preserved by conservation easement which created buffer zones along the course of the creek and its tributaries in which all building was prohibited. This would protect woodlands, steeper slopes, and flood plains along streams whose natural filtering action and stabilizing effect on the water table are important to stream quality.

The water quality was to be preserved by the phased installation of a sewage system and sewage treatment facilities to replace individual septic tanks. Increased population was to be accommodated by cluster developments in areas not restricted by easements. Under the easement system a landowner retains his property but sells his right to use the land in the ways forbidden by the easement. The cost is simply the value of the property with and without the easement. The estimated cost of the easements to be purchased was set at about three million dollars.

This approach to land protection would work if 80 per cent or more of the landholders agreed to sell easements. If not the County could compel this sale by writ of eminent domain. The plan was taken to the people. At first it met with apathy, then antipathy and much misunderstanding of the plan. Soon there developed growing acrimony and resistance. Some of it was due to the residents' previous experiences with pipeline, power-line, flood

control projects in which eminent domain was invoked with little attention to local interests or feelings. Such seizures had been fought to no avail by the residents. In one case a bulldozer was stopped even at gunpoint.

It is not surprising why the writ of eminent domain contemplated in the Brandywine Plan precipitated such a glandular reaction against the Plan as a whole. The more the Plan was explained the more resentment it encountered. "Intellectuals" were telling outsiders what to do. It was another land grab. Duponts were behind it, etc. The residents then formed their own Commission to develop an alternative, embracing the same goals but which achieves them through local ordinances rather than easements.

The residents seem under the illusion that the present priority is due to their own "wise" land management practices over generations. They resent the two industries which are presently polluting the Brandywine and attribute this to the weakness of the County authorities who allow them to continue to operate without proper effluent treatment. Furthermore, the residents believe Pennsylvania has all the laws necessary to protect the basin and that it is higher levels of government in league with "special interests" that have defaulted on their obligation to enforce laws. Now they think it is time for local government to take over!

So now the IES plan is dead, and there will be much land speculation. If a plan based on local police power ever comes to pass, it will be years away and much more expensive. The plan on Brandywine was not altogether wasted, however, because it is already serving as a model for the development of watersheds in other regions of Pennsylvania and the Northeast. A real lesson did come out of the whole experience. It is one in human relations, one element being individual greed. There was also a confrontation between "intellectuals" and rural Americans who reacted not intellectually to their collective best interests, but emotionally even against themselves. These are valuable base-line data for future attempts to preserve our Country.

There are, of course, other challenges to water purity besides the people themselves. Federal bureaucracies and Congress as well as the communities which live on the river shores. In the case of the Potomac which was once a sparkling stream in which President John Adams once swam, it is now ruined and reeking. Among the worst offenders, states the New York Times,³ are Federal agencies

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References: 1. Vernier, R. L., in Patient Care Feature: *Patient Care*, 1:20 (Feb.) 1967. 2. Beeson, P. B.: "The Infectious Diseases," in Beeson, P. B., and McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Philadelphia, W. B. Saunders Company, 1967, p. 230.

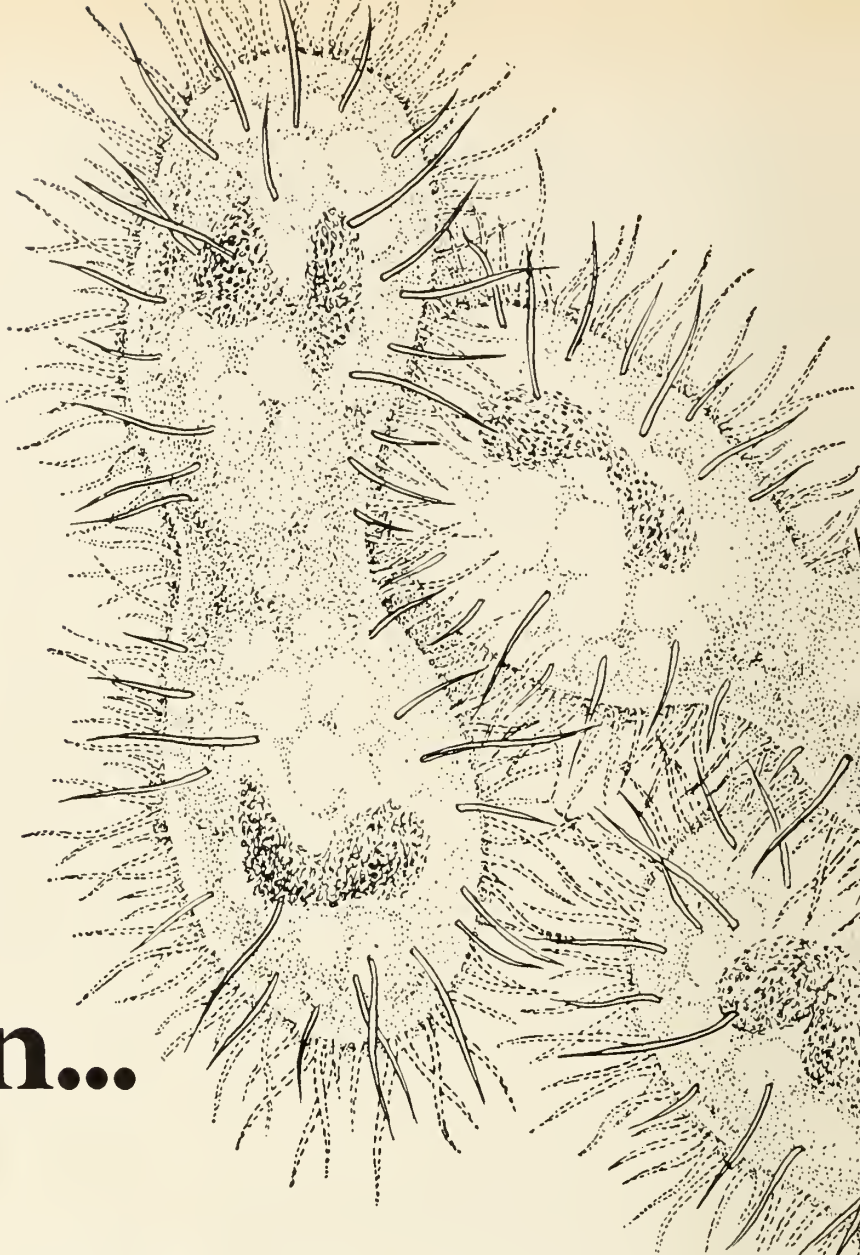
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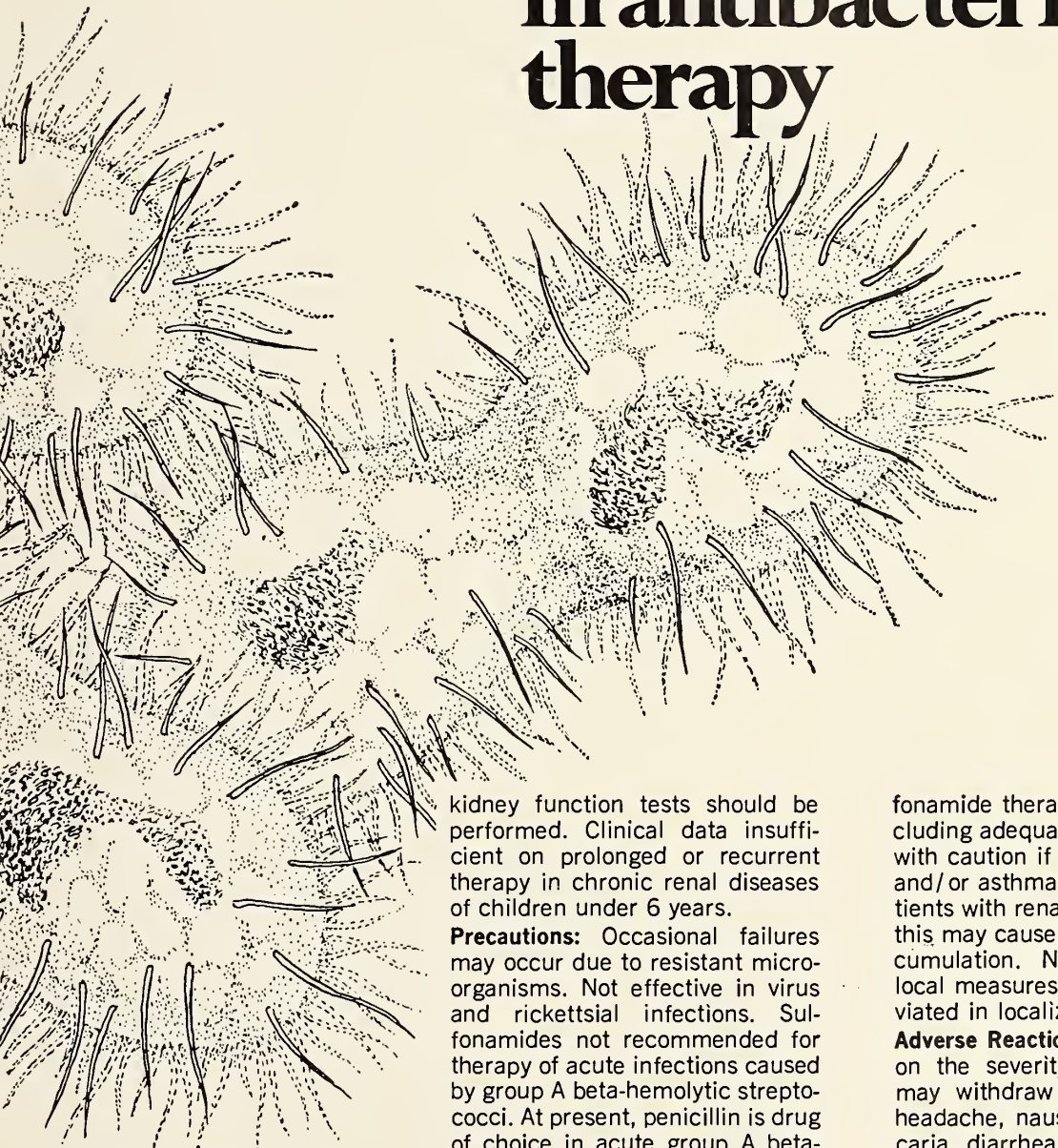
sue infections due to susceptible microorganisms; prophylactically following diagnostic instrumental procedures on genitourinary tract.

Contraindicated in sulfonamide-sensitive patients, pregnant females at term, premature infants, or newborn infants during first 3 months of life.

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fonamide therapy precautions, including adequate fluid intake. Use with caution if history of allergies and/or asthma. Follow closely patients with renal impairment since this may cause excessive drug accumulation. Need for indicated local measures or surgery not obviated in localized infections.

Adverse Reactions: Depending upon the severity of the reaction, may withdraw drug in event of headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, Stevens-Johnson syndrome, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.



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such as the Defense Department and the Central Intelligence Agency which do not provide enough sewage treatment for their installations. Congress is to blame for not approving enough money to do all that needs doing. Virginia and Maryland have been equally delinquent in not heavily subsidizing towes along the Potomac to build sewage treatment plans.

The importance of reclaiming this already mined river receives fine words but no action from the Administration so far. The magnitude of the problem to preserve our Country can be seen in the two examples cited above. On the one hand is a lack of community spirit and understanding by the citizen, and his suspicion of government agencies. On the other is indifference by the Government and Congress to preserve the beauty of our landscape and the purity of our streams.

L.H.N.

References

1. The Plan and the Program for the Brandywine. Institute for Environmental Studies, University of Pennsylvania, 3400 Walnut Street, Philadelphia, 19104. \$3.50.
2. Thompson, P.: Brandywine Basin: Defeat of an almost perfect plan. *Science*, 163: 1180, 1969.
3. Ruined River. *New York Times* Editorial. p. 34, April 12, 1969.

The Problem Of Chemical Mutagenesis

Do nontoxic chemicals and drugs present a hazard to the population by causing mutations or other disturbances in genetic function? How serious is the clinical problem due to mutations resulting from human exposure to drugs, pesticides and other chemicals? Is there any way at present to relate to man the mutagenicity due to chemical agents observed in organisms such as bacteria and insects? How feasible is it in the present state of our knowledge to develop rapid inexpensive and accurate tests to predict the hazard of any specific chemical in producing mutations in man? These questions were taken up at a meeting in May 1968 at Bethesda by eleven scientists.¹

Out of the discussions on radiation hazards ten to fifteen years ago came the public policy for control, the ratio of benefit to hazard being the decisive factor. In the case of radiation the mechanisms of possible control were relatively simple and one could extrapolate from one organism to another with reasonable confidence. But this does not appear to be true with respect to a variety of chemicals to which the population is exposed. We could attempt to identify compounds as being mutagenic by laboratory tests. We could also try to detect in some way the existence of something affecting the human mutation rate and then determine what is causing the change.

Thus far there is no example of harmful effects in man which can be attributed to mutation resulting from exposure to a specific drug or chemical. Does this mean that no clinical problem exists. The possibility cannot be dismissed because we know some common substances can cause mutations in bacteria and insects. Furthermore, some new experience might emerge suddenly as in the case of the teratogen thalidomide. Furthermore there will continue to appear new drugs such as antimetabolites used in non-malignant disease and the likelihood of use of immunosuppressive agents in auto-immune diseases. For this reason continual alertness for the possibility of mutagenesis is mandatory.

We should not wait for some obvious and perhaps catastrophic demonstration of chemical mutagenesis in humans to occur. Perhaps epidemiological studies could be carried out with some reasonable expectation of detecting increased genetic disease, and then associating it with some particular drug. Data could be obtained on offspring of persons known to have been exposed to certain specific compounds such for example workers in

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DDT manufacturing. Another such compound is atabrine which interacts with nucleic acids and is subsequently found in tissues in concentrations of a thousandfold higher than in plasma. Vast numbers of persons in malarious areas were given the drug during World War II and now their offspring are available for study.

The problem is highly complex because the distribution of a drug, its metabolic products, cellular concentration in various organs varies. Furthermore, interpretation of many obvious easily recognized genetic alterations is still uncertain. The significance or importance of chromosome breaks which have been observed in human cells is still unknown. The problem is further compounded by the possibility that some substances which are not mutagenic in themselves might be converted into mutagens metabolically or prove to be so in combination with other factors such as drugs, agricultural chemicals, radiation, etc. For example caffeine by itself is not a strong mutagen in bacteria but in the presence of ultraviolet light mutations are observed perhaps because of an inhibitory effect of caffeine on the genetic repair mechanism.

The conclusion of the conference was that no laboratory or clinical tests are now available for predicting a mutagenic hazard in man with any degree of certainty. It was agreed that to condemn a useful or potentially useful drug on the basis of any single available test would be a disservice. However, there is reason to believe that in time such tests can and will be developed. Studies of chemical mutagenesis in the mouse are being conducted and these bear watching. M. Legator of the FDA described his host-mediated test which represents an attempt to utilize an invitro system in an in-vivo situation. In this test the drug is administered to the mouse and then a bacterial suspension is introduced into the peritoneal cavity. Later the bacteria can be examined for mutagenic changes. The mouse-dominant lethal test appears capable of picking up selected types of compounds but no one test is satisfactory for the purpose. It will be necessary to utilize a gallery of screens in order to obtain satisfactory answers.

Technological advances can be expected to increase the speed and accuracy of scanning cell populations. Before interpretations are made, however, we need to know more about the significance of genetic alterations. What does a chromosome break mean? Are all breaks initiated the same way? Are some mutations due to failure to repair? Are mutations due to direct damage of the nucleic acid or to

breakage of protein back-bones or to secondary factors? Are all breaks harmful?

Obviously more basic work on mechanisms and interpretation of genetic alterations is needed. For this we will need more trained pharmacologists in the field of genetics, in order to extend basic findings to the practical level of human utilization.

L.H.N.

References

1. Heming, A. E. and Brown, J. H. V.: Chemical mutagenesis. *Science*, 163: 1361, March 21, 1969.

Exocrine Immune Gammaglobulin

A growing body of evidence suggests that the presence of immune gammaglobulin A (IgA) in local respiratory secretions may be a more important index of host resistance to certain viral infections of the respiratory tract than are circulating antibodies. During the acute infection of course interferon, a low molecular weight protein apparently plays a key part in the limitation of virus replication within cells already infected and in the protection of nearby and distant cells from the spread of the infection. IgA appears to be the predominant immunoglobulin with specific antibody activity present in exocrine secretion.

Smith et al¹ showed that the presence of type specific local antibody to para-influenza Type I virus provided a more reliable index of resistance to infection by that agent than did the presence of homologous serum antibody. Conversely susceptibility to infection has correlated most reliably with the absence of such a local antibody. Recently Agra et al² presented data suggesting that a similar situation obtains in the gastrointestinal tract where their studies of IgA in duodenal fluids possessed specific poliovirus antibody. It would seem, therefore, that induction of serum antibody alone may be an inadequate assessment of certain viral vaccines.

Bellanti et al³ in their report on measles virus immunity have given us another example of the direct correlation of the resistance of the respiratory tract to infection with the presence of local secretory antibody IgA. The children immunized with inactivated virus showed little production of local exocrine antibody whereas those vaccinated with attenuated vaccine showed active local production of IgA globulin. The attenuated measles virus vaccine produced an immune state similar to that seen after active viral infection whereas inactivated measles virus vaccine seemed to stimulate only the serum antibody selectively.

These studies help one to understand two clinical observations. The first is undue susceptibility to recurrent respiratory tract infections that had been noted in persons who are unable to produce specific local IgA. For example patients with ataxia telangiectasia⁴ lack respiratory IgA and this deficiency is accompanied by frequent pulmonary infections. Investigation of other presently uncategorized patients who undergo recurrent respiratory tract infections may be expected to reveal additional deficiency syndromes in which alterations of the IgA defense system correlates with an undue susceptibility to respiratory pathogens.

The second area is the better understanding of vaccine efficiency. Naturally acquired viral infections and those resulting from attenuated virus vaccines were both followed by the appearance at local sites of specific antibody in the IgA form. However, after the administration of inactivated vaccines prepared from the local viruses, local respiratory tract or gastrointestinal tract antibody was rarely detectable even though there appeared in the serum antibodies at levels comparable to those that followed live virus infection.

This discrepancy between humoral and local defenses may apply to other viruses that invade via the respiratory or gastrointestinal mucosa. It would seem self-evident that vaccines that stimulate serum antibody selectively without local mucosal antibody should not be used. Therefore, in the development and evaluation of vaccines for immunization more attention may now be directed to vaccines and routes of administration that can be relied upon to stimulate production of local secretory IgA.

References

1. Smith, C. B., Purcell, R. H., Billant, J. A. and Chanock, R. M.: Protective effect of antibody to para-influenza type I virus. *New Eng. J. Med.*, 275: 1145, 1966.
2. Agra, P. L., Karzon, D. T., Righthand, F. and Mac Gillivray, M.: Immunoglobulin response in serum and secretions after immunization with live and inactivated polio vaccine and natural infection. *New Eng. J. Med.*, 279: 893, 1968.
3. Bellanti, J. A. et al: Antibody response in serum and nasal secretions to measles vaccine. *New Eng. J. Med.*, 280: 628, March 20, 1969.
4. South, M. A., Cooper, M. D., Wollheim, F. A., and Good, R. A.: IgA system II clinical significance of IgA deficiency: studies in patients with agammaglobulinemia and ataxia telangiectasia. *Am. J. Med.*, 44: 168, 1968.

Prenatal Diagnosis Of Hereditary Disorders

Recent advances in the treatment of some genetic disorders have brought some hope to victims of

these disorders and to their families. Notable examples are the dietary management of phenylketonuria and galactosemia and improved factor VIII preparations in the treatment of hemophilia. However, for many seriously disabling disorders there is no treatment and all that can be offered to a family is genetic counselling, that is advising the parents of the approximate risk that they will have a defective child. Now, however, geneticists are able to make exact prenatal diagnosis for several inherited disorders. In essence fetal cells desquamated into the amniotic fluid are obtained by amniocentesis and then grown in cell culture. In this way it is possible to obtain a preview of the chromosomes and enzymes of the child.

Amniocentesis at sixteen weeks gestation has a low morbidity for both fetus and mother¹ and when indicated, abortion can be done with hypertonic saline as late as twenty-four weeks gestation. The method can provide a firm diagnosis of all chromosome disorders such as Down's syndrome (mongolism) which can be detected by karyotype analysis. Analysis of hormones in the amniotic fluid has also allowed for the diagnosis of adreno-genital syndrome. Biochemical studies of cultures derived from amniotic fluid cells have shown the practicability of prenatal diagnosis of a number of hereditary metabolic disorders. The rapid progress in this area has been documented in a recent review by Nadler.²

Perhaps amniocentesis could be carried out routinely in older pregnant women that had been exposed to an increasing risk of delivering a mongoloid infant and some day even on mothers exposed to viruses and other chromosome breaking agents when the effect of these lesions become better understood.³ Most inherited disorders may show themselves in some subtle way in these fetal cells including it is hoped disastrous dominant traits such as osteogenesis imperfecta and tuberous sclerosis.

Fratantoni et al⁴ described two cases, one of Hunter and one of Hurler's syndrome that they were able to diagnose from cultured amniotic fluid cells. Both of these hereditary disorders are variants of mucopolysaccharidoses. Both produce retarded growth and mentation, characteristic facies, skeletal abnormalities, cardiovascular involvement and early death. Biochemically the conditions are characterized by storage in tissues and excretion in the urine of two mucopolysaccharides. Skin fibroblasts cultured from patients with these disorders store sulphated mucopolysaccharides which can readily be detected by the way the cells stain and by the way they accumulate radioactive sulphate in cellular

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mucopolysaccharides. In Hurler's syndrome the diagnosis was made in time to allow therapeutic intervention.

Additional diagnostic information may be expected when there has been established the definition of normal concentrations of metabolite and enzymes in the amniotic fluid. Then enzymes that back up behind an enzymatic block may not be completely cleared from the fluid by the mother. However, normal values in cells and fluid will not be easy to establish. Then there are the metabolic disorders which are manifested by cytoplasmic granules which stain in metachromatic fashion, a remarkable discovery with wide implications.⁵ However, these are variable and slow to appear in culture. It is difficult to distinguish one of these disorders from another in the present state of our knowledge or even heterozygous carriers from affected homozygous persons.

It is obvious as Littlefield⁶ points out that the diagnosis must be as conclusive as possible. Each will depend on a laboratory test which will have to be performed with unusual care and monitoring, and interpreted most expertly. It might be that only a few laboratories in the country will cooperate in such a venture to perform the analysis for rare disorders involving unusual enzymes. Obviously prenatal diagnosis will constitute a major medical advance only if treatment can be given once the diagnosis has been made.

Perhaps the time will come when occasionally there may be possible prenatal therapy for the fetus as suggested by Fratantoni.⁷ Now, however, both society and the profession must appreciate and accept the fact that the proper therapy, which at times will mean abortion, is in the interest of the parents and also society that often is burdened by hereditary disorders. Obviously when a disorder cannot be diagnosed with confidence or can be treatable to some extent there will always be some who will elect to continue the pregnancy. However, when a disorder inevitably will cause mental or physical incapacitation, the alternative of therapeutic abortion should be lawfully available as it already is in some states. Actually it would not be "therapeutic" in any sense of protecting the life of the mother, but certainly it would be a boon to the family as well as society.

The world is not in need of those who are unable to compete thereby placing an unhappy burden on parents and societies. Both parents and society are

entitled to children who are healthy rather than defective.

L.H.N.

References

1. Creasman, W. T., Lawrence, R. H. and Thiede, H. A.: Fetal complications of amniocentesis. *JAMA*, 204: 949, 1968.
2. Nadler, H. L.: Prenatal diagnosis of genetic defects. *J. Pediat.*, 74: 132, 1968.
3. Gorman, J.: Human chromosomal breakage. *J. Pediat.*, 72: 440, 1968.
4. Fratantoni, J. C., Neufeld, E. F., Uhlendorf, B. W. and Jacobson, C. B.: Intra-uterine diagnosis of the Hurler and Hunter Syndrome. *New Eng. J. Med.*, 280: 686, March 27, 1969.
5. Danes, B. S. and Bearn, A. G.: Hurler's syndrome: genetic study in cell culture. *J. Exper. Med.*, 123: 1, 1966.
6. Littlefield, J. W.: Prenatal diagnosis and therapeutic abortion. *New Eng. J. Med.*, 280: 722, 1969.
7. Fratantoni, J. C., Hall, C. W. and Neufeld, E. F.: Hurler and Hunter syndromes: mutual correction of defects in cultured fibroblasts. *Science*, 162: 570, 1968.

Gaps In Doctor-Patient Communication

Medical care is increasingly complex and fragmented and the warmth of a long term association with a single physician has become a luxury for a few rather than the customary setting for the delivery of health care. What then do we know about the interaction between doctor and patient which influences the patients responses to what his physician told him. In a recent communication this question was subjected to a detailed analysis of verbal communication between physician and patient in a pediatric clinic. It furnished data on patient satisfaction with medical visits and also documented the extent to which patients followed medical advice.

Most studies in the past agree that compliance by the patient is related to the nature of the regimen prescribed. Prescription of medicine are easy to comply with but restriction of behavior and changes in personal habits are difficult to comply with. In what way does the doctor-patient relation affect compliance. In the Los Angeles Clinic¹ 42 per cent of 587 patient visits resulted in high compliance, 38 in moderate and 12 per cent in no compliance. If the patient's expectations were unmet, the compliance was very low. Friendliness and warmth on the part of the doctor as perceived by the patient played some role in the patient's satisfaction but did not in itself result in increased compliance. However, if the doctor did not "seem" friendly there was a significant reduction in compliance. Likewise, if the patient "thought" that the doctor did not understand her concern over the child's ill-

ness compliance went down. Clearly it is necessary for the physician to show concern for the patient's feelings and to understand them.

One-quarter of all patients were dissatisfied and three-quarters were satisfied. It turned out, however, that the relation between satisfaction and compliance is not a simple one. A large number of highly satisfied patients failed to follow through on any of the recommendations while others highly dissatisfied with their visits yet followed all the doctor's instructions. If the mother perceived the illness to be "very serious" there was a slight increase in patient compliance.

Two factors did correlate statistically with non-compliance. One was when three or more medicines were prescribed and when medicines as well as treatments were prescribed. Apparently many patients have difficulty in following too many and too complicated instructions. Another factor in non-compliance was when an interval of over seven days occurred between initial and follow-up visits. This finding has great relevance in treating chronically ill people who if they are not seen often enough will fail in compliance and suffer reverses in health. This is especially true with patients taking four or more drugs at one time.

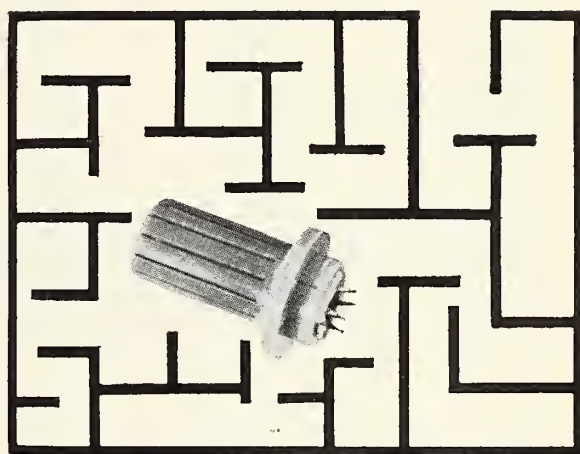
Frances' and his coworkers study indicates that the seriousness of the illness as perceived by the mother, the complexity of the instructions that are offered and the practical circumstances in which the patient finds himself in his home environment, all have considerable influence on the degree to which medical advice will be followed regardless of what takes place in the communication with the doctor. Furthermore, that compliance reflects the measurable attributes of the doctor-patient interaction less sensitively and less accurately than patient satisfaction might have been anticipated. There are many forces that motivate health behavior and patient cooperation besides what is done or what is said by the physician.

An actively unpleasant manner on the part of the doctor and even his assistants affects cooperation adversely, whereas extra warmth and friendliness lead to increased satisfaction, but have no measurable effect on follow through with medical advice. In view of the fact that some investigators have proposed that increased social distance between doctor and patient makes for greater compliance, it is worth noting that lack of warmth to the extent that it affected compliance at all did so in a negative way.² One can speculate that in long-lasting warm relations between doctors and indi-

vidual patients attributes of the doctor-patient interaction might be found that do affect compliance. In internal medicine and family medicine as well as pediatrics there is much experience that certainly suggests that a long-lasting relation felt, in itself makes for increased compliance.

It had seemed likely that the kind of illness and the doctor's actual diagnosis would be strong determinants of follow through on medical advice. This is true only if the patient's ideas concerning the seriousness of the illness were an outcome of the consultation so that the doctor's diagnosis and the kind of illness was understood and accepted by the patient. In Frances' study the doctor's ideas concerning the presenting problem and the health threat that it poses did not influence the mother's motivation as much as her own perception of the illness. Doctors must, therefore, be aware of the failure of communication and the exact explanations that are necessary to motivate the patient to compliance.

Other factors that have previously been linked with failure of the patient to follow medical advice such as social disorganization in the home, the number of siblings and parent's education while not significant in the present study might be more



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important in a different situation.³ It is conceivable that certain families more than others can muster sufficient resources, organization and motivation to comply with short term relatively simple courses of treatment and yet fail in long term cooperation. It might be that the patients educational level and understanding of the reasons for the measures could be shown to be of strong influence.

What it all adds up to is that the doctor-patient relationship is a very complex one as far as carrying out instructions is concerned. They must be simple, clearly understood, and the patient's perception of his illness is primary in following instructions. The physician must convey to the patient his concern for his suffering and must communicate with the patient in such a way that no gap exists between what the doctor says and what the patient understands him to say.

L.H.N.

References

1. Frances, V., Korsch, B. M. and Morris, M. J.: Gaps in doctor-patient communication: patients response to medical advice. *New Eng. J. Med.*, 280: 535, March 6, 1969.
2. Davis, M. S. and Eichhorn, R. L.: Compliance with medical regimens: panel study. *J. Health and Human Behav.*, 4: 240, 1963.
3. Davis, M. S.: Physiologic, psychological and demographic factors in patient compliance with doctors' orders. *M. Care*, 6: 115, 1968.

The Teacher's Role In Student Motivation

Let the main objective be as follows, to seek and find a method of instruction by which teachers may teach less but learners may learn more. — The Great Didactic of Comenius (1592-1670). Johann Amos Comenius, *Encyclopedia Britannica*, 6: 132, 1964.

What is it that motivates one to learn and continue to learn. Educators in medicine like educators in general are at times inclined to the view that motivation is something a student has or does not have in his make-up. But he is obviously motivated in having as his goal becoming a physician for which he must become proficient in the various subjects needed to become a good physician. If the students effort and performance should fall off, we glibly come to the conclusion that there is something wrong with his interest or his motivation. But is this necessarily true. How does this view square with what we already know about the psychology of motivation and learning.

The major determinant of performance is the long range purpose or career goal of the student

and this plays a role in his choice when faced with a number of educational curricula. Beyond that, however, it does not seem to play a big role in the day to day, lecture to lecture effort and learning of most students. To stimulate day to day effort, things must be presented to the student in an interesting way. This means that day to day motivation, the effective motivation for learning is largely the educators responsibility and not that of the students.

Students, of course, bring some qualities to the learning situation. They require ability to attend and concentrate and sustain these over long periods. They require the ability to memorize and store large amounts of information. They must be able to think through complex problems. All these are necessary conditions for effective learning. But they are not sufficient. These abilities and skills will not be activated and sustained in action unless there is motivation. For example how many students will spend hours trying to digest difficult material which will not be on any examination according to the teacher, since it is not relevant to medical research or practice. Probably none. Motivation is a necessary condition for learning and performance and it usually hinges on factors outside a person.

To have a motive implies that the person has a purpose or goal, something he is seeking to acquire like food, money, attention, approval or prestige. It may also be something he is seeking to escape from or avoid like pain, discomfort, boredom, threat, anxiety or failure or loss of face. It may be some activity he wants to engage in for its own pleasure such as social behavior, or exploratory and problem solving behavior. In a single short term situation if the individual has a particular motive or goal he will work and learn to attain that goal.

Effort towards a goal and behavior need to be reinforced. If attainment of any goal does not follow as a consequence of behavior then the behavior will be extinguished. It follows that effort and learning behavior will be maintained and increased only if the outcomes are positive and appropriate to the individuals goals. Most of these outcomes or reinforcers must be delivered by the physical and especially the social environment.

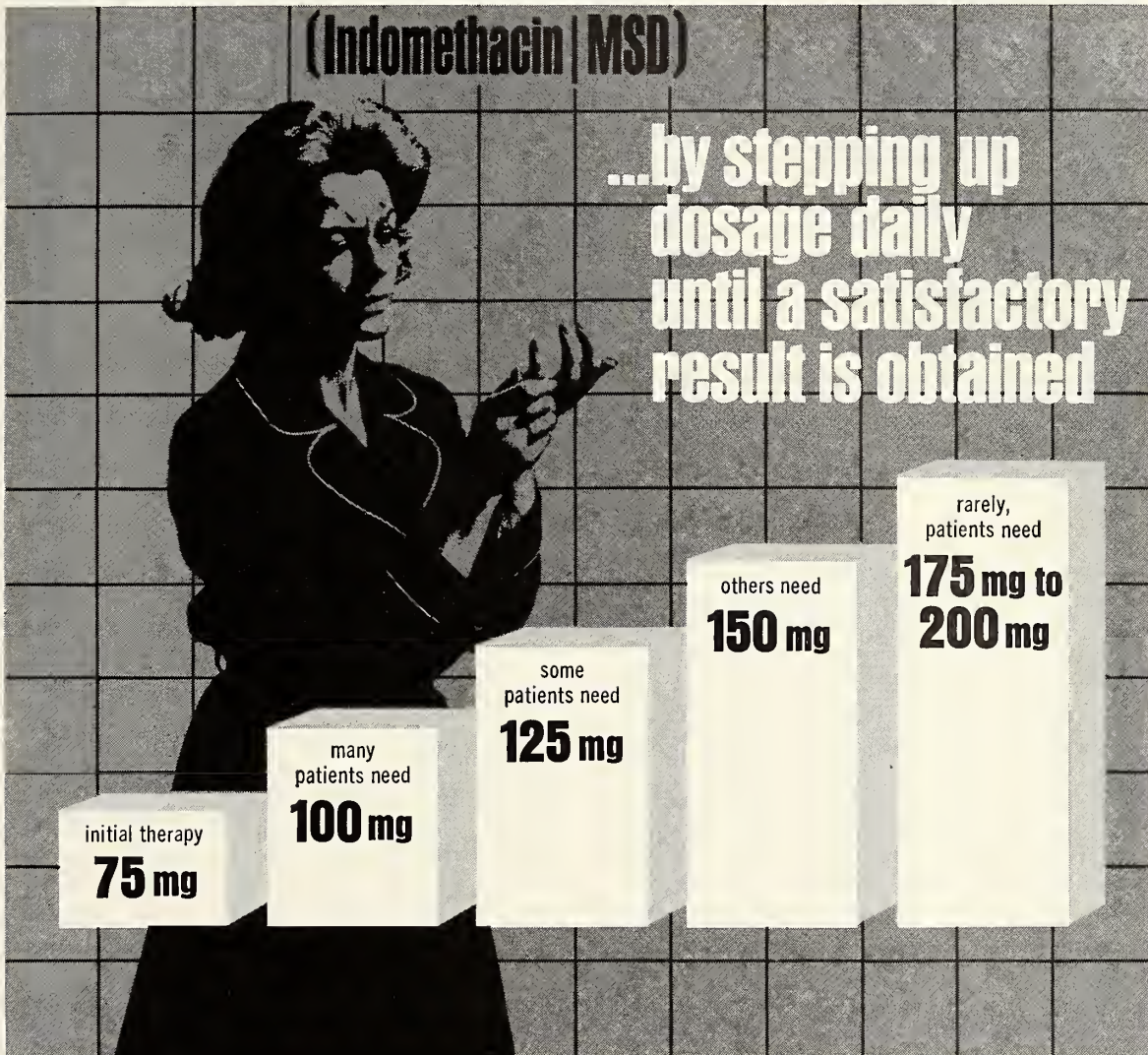
Motivation is a major problem for students because the motivation is complex and long-term. The student may have the goal of becoming a physician, but that motive in itself does little more than determine the behavior at the point of choice

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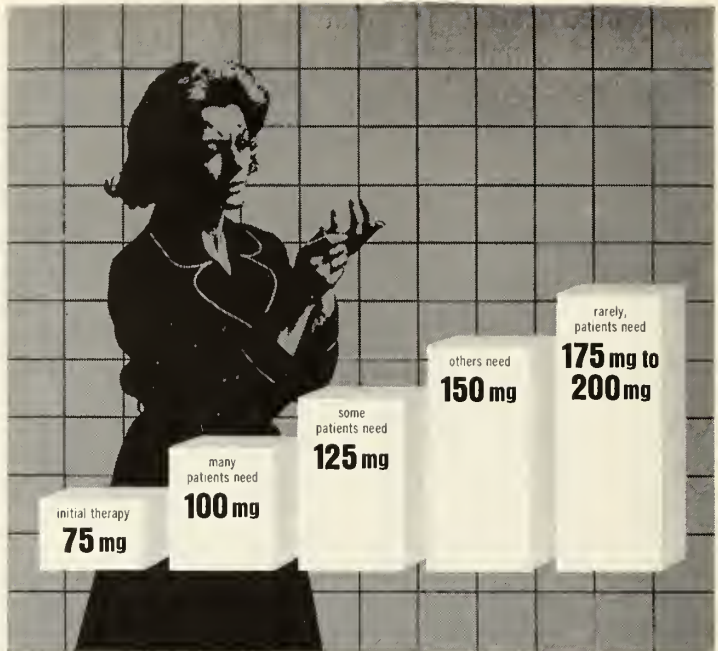
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- in children
- INDOCIN may mask the signs and symptoms of peptic ulcer and may cause ulceration or irritation of the G.I. tract. Therefore, do not give in active peptic ulcer, gastritis, regional enteritis, ulcerative colitis, and use with caution if there is a history of these disorders.

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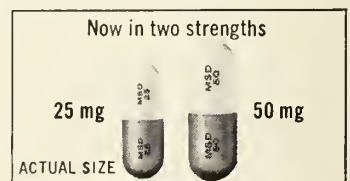
Precautions: Use cautiously in patients with a history of peptic ulcer, gastritis, regional ileitis, or ulcerative colitis because of its potential for causing G.I. bleeding. May cause single or multiple ulceration of the esophagus, stomach, duodenum, or small intestine, and, in a few instances, severe bleeding and perforation with a few fatalities have been reported. May potentiate the ulcerogenic effect of steroids, salicylates, or phenylbutazone. Gastrointestinal bleeding with no obvious ulcer formation has also been noted; the drug should be discontinued if G.I. bleeding occurs. As a result of obvious or occult G.I. bleeding, some patients may manifest anemia, and for this reason periodic hemoglobin determinations are recommended. G.I. effects may be minimized by giving the drug with food or with antacids or immediately after meals. In common with other drugs that have anti-inflammatory, analgesic, and antipyretic properties, indomethacin may mask the signs and symptoms of infection; avoid undue delay in initiating appropriate treatment of the infection; use cautiously in patients with existing, but controlled, infections. As with any new drug, patients should be followed carefully to detect unusual manifestations of drug sensitivity.

Adverse Reactions: Starting therapy with low doses, with gradual increases when necessary, will minimize adverse reactions. **Central Nervous System:** Most commonly, headache (usually more

severe in morning), dizziness, and lightheadedness; infrequently observed reactions include mental confusion, drowsiness, convulsions, coma, depression, and other psychic disturbances, such as depersonalization; CNS effects are often transient and frequently disappear with continued treatment or reduced dosage. The severity of these effects may occasionally require cessation of therapy. **Gastrointestinal:** Most commonly, nausea, anorexia, vomiting, epigastric distress, abdominal pain, and diarrhea; others that may develop are ulceration, single or multiple, of esophagus, stomach, duodenum, or small intestine, including perforation and hemorrhage with a few fatalities having been reported; G.I. bleeding without obvious ulcer formation, increased abdominal pain in patients with preexisting ulcerative colitis; less commonly, stomatitis; gastritis; bleeding from the sigmoid colon, occult in type or from a diverticulum, and perforation of preexisting sigmoid lesions (diverticulum, carcinoma); G.I. reactions not known definitely to be attributable to indomethacin include development of ulcerative colitis and of regional ileitis. **Hepatic:** Rarely, jaundice and hepatitis. **Cardiovascular-Renal:** Infrequently, edema, elevation of blood pressure, and hematuria. **Dermatologic-Hypersensitivity:** Infrequently, pruritus, urticaria, angioneurotic edema, angitis, skin rashes, loss of hair, and acute respiratory distress including sudden dyspnea and asthma. **Hematologic:** Infrequently, leukopenia, purpura, and thrombocytopenia; rarely, agranulocytosis and bone marrow depression have been reported, but a definite relationship to the drug has not been established; since some patients may manifest anemia secondary to obvious or occult G.I. bleeding, periodic hemoglobin determinations are recommended. **Eye-Ear:** Infrequently, tinnitus, blurred vision, hearing disturbance, and orbital and periorbital pain. **Miscellaneous:** Rarely, vaginal bleeding, hyperglycemia, and glycosuria.

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of selecting the medical program. If effort and learning are to be sustained from that point onward various submotives or subgoals with their appropriate outcomes must be introduced systematically by the teachers. One of the most important motivations seems to be the examination.

The desire to achieve followed by the reinforcement of achieving, the threat of failure followed by the reinforcement of relief from the threat, are strong motives for concentrated effort and learning. This is especially true if the examinations count as a hurdle on the way to a long-range goal. Examinations may also be used as a self-evaluation instrument as in programmed instruction. It offers intensive reinforcement and creates a need in the student to learn more at the same time giving the teacher a measure of the effectiveness of his teaching. Examinations then, however performed are not simply measuring devices but in fact are powerful instruments for motivating behavior, for directing behavior towards the objectives of the course and for providing corrective feedback.¹

A second motivator is the relevance of the topic to medical practice and research.¹ It cannot be assumed that this will be obvious to the student. It must be made explicit perhaps by devising ways of confronting the students with the outcomes for a patient if relevant information is neglected or misused!

A third motivator is curiosity and problem solving. Because these are often suppressed in our educational system it is especially urgent that they must be activated by the teacher by his planning and pointing out gaps, discrepancies and contradictions in information, theory and practice.

It is not the student, but the teacher who must introduce and use all possible motivations, for motivation in medical education is largely the responsibility of the teachers in medicine.²

L.H.N.

References

1. Nahum, L. H.: A new science of learning: programmed instruction. *Conn. Med.*, 29: 153, March, 1965.
2. Motivation and learning. *Can. Med. Assoc. Jr.*, 100: 623, April 5, 1969.

Examining The Examiners

Christine McGuire¹ in reviewing the whole subject of professional assessment makes the reasonable claim that we should include more than the ability to recall learned information. It should embrace also skill in the interpretation of data in the analysis and evaluation of situations and also in

the making of decisions. Accordingly she describes entirely new techniques which could replace whatever patients happen to be available for examination purposes. Simulated clinical situations she thinks could be devised which are reproducible for the whole group of students. Of course, such tests require for their planning considerable time and the exercise of much ingenuity and imagination on the part of the examining body. Clearly this is a far cry from the haphazard approach that was once the rule.

Others have become aware of this and the medical curriculum has been studied and criticized in depth. All seek to render the medical students training relevant to the situations he can expect to encounter in practice as well as to take account of the extraordinary expansion in biomedical knowledge. Accordingly not only the subject matter and form of the instruction have been under scrutiny, but also the conventional methods of appraising the student's knowledge and skill. These are recognized by most teachers as being less than satisfactory and innovations will continue to be introduced. For example the essay type of examination paper is being widely replaced by a multiple choice form of test because it is believed to provide a more accurate evaluation of the candidates knowledge. Most recently the clinical examination has also come under attack.

Most doctors who have served as clinical examiners will admit that the traditional oral and clinical examination can be quite inadequate and even unfair means of judging a student's ability. It happens that there is too large an element of luck involved as regards not only the patient that was assigned to the candidate but also the examiner who is not without his pet topics and personal idiosyncrasies. Accordingly we find that information about the examiners personal preferences and vagaries is passed around among students and it was generally acknowledged that a good examinee was one who could best please the examiner.

The grounds for the dissatisfaction with the clinical examination have a factual basis which is borne out by a study conducted in Glasgow by G. M. Wilson et al² and reported in *Lancet*. Final year students were given an hour to take a history from and then examine a patient with multiple sclerosis who displayed clear-cut physical findings of that disease. Each of the students was questioned by an examiner in the presence of a second examiner both of whom assigned a mark independently. The proceedings were recorded on videotape. These

topics were re-marked by the same two examiners two weeks and two months afterwards.

In addition they were shown to twelve other teachers of differing degrees of seniority. The results of the re-marking did not differ greatly from the mark originally assigned. However, when the marks awarded by the fourteen examiners were scrutinized it was found that no candidate showed a variation of less than ten marks between the top and bottom scores. In thirteen it was fifteen marks, in three it was twenty and in one it was twenty-five. In no case did all examiners award fail marks to a candidate while fifteen students were failed by at least one.

The mean mark of the fourteen examiners was below fifty in only six, so that nine of the fifteen who might have failed actually deserved to pass. At the other end of the scale candidates awarded a distinction by some examiners received only a pass by others. It must not be forgotten that the circumstances were uniform for all students being examined and that the discrepancies in marks would be greater under the usual conditions when a number of patients presenting features of a widely different complexity are utilized in the examination.

Confirmation of the variability in marking also appears in the report by Waugh and Moyse. Here again the oral examination, in this instance in pathology were recorded on videotape and marks were independently assigned by a number of examiners. There is here the additional feature that marks for oral and multiple choice tests were compared. Some striking discrepancies came to light. Marks differing by as much as 15 per cent were awarded although the mean grade given by subsequent viewers was not greatly different from that of the original examiners. There was, however, greater likelihood of agreement in the case of the best candidates and the poorest.

To all that have an interest in medical education by conclusions which emerge from such studies as these, it will be apparent that there is need for greater objectivity and accuracy in assessing student achievement. The deficiencies of the established methods revealed above extend far beyond medical education into the examinations for specialty board qualification. The old methods failings should not upset those examiners too much since they cannot be themselves examined in the absence of videotape recordings.

L.H.N.

References

1. McGuire, C. H.: A scientific approach to problems of professional assessment. *Can. Med. Assoc. J.*, 100: 593, 1969.
2. Wilson, G. M. et al: *Lancet*, I: 37, 1969.
3. Waugh, D. and Moyse, C. A.: Oral examinations: A video tape study of reproducibility of grades in pathology. *Can. Med. Assoc. J.*, 100: 635, April 12, 1969.
4. The clinical examiner examined. *Can. Med. Assoc. J.*, 100: April 12, 1969.

The Role Of The Biogenic Amines In The State Of Sleep

In the past ten years the study of sleep mechanisms has developed very rapidly once an objective method became available for studying this phenomenon. As a result of intensive study four major concepts have emerged which have changed the classical theory of sleep. One is that far from being a passive phenomenon sleep is actually a very active phenomenon. It can be induced by electrical stimuli at different parts of the brain including those which overlap the ascending reticular activating system. The stimulation, however, must be of low frequency which must correspond to the frequency of the sleep spindle. In contrast one can produce total insomnia by destroying these areas.

The second concept arose from the recognition that the mammalian brain actually passes through two states which can be easily recognized. The initial state is slow-wave sleep. The eyes are closed, pupils are myotic, the postural tonus of some muscles remains and the electroencephalogram reveals slow waves and spindles. This state soon goes into paradoxical sleep with cortical activity similar to that in the waking state. There is now total absence of electromyographic activity except in some of the neck muscles. There is phasic activity with rapid eye movement (REM) similar to that recorded during visual attention. The suggestion, of course, is that during this state of sleep active phenomena are at work triggering electrical events and REM. It is important that certain drugs can dissociate these two states.

The slow wave phase of sleep is a function of maturity of the central nervous system. Newborn infants with incompletely developed C.N.S. go only from waking to paradoxical sleep. When maturation of the cortical network is achieved, then slow-wave sleep appears. The paradoxical sleep is also not present in all animals. For example fish and reptiles are without it. It is of very short duration in birds but it is present in man and all mammals studied. Thus we have evolved

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two quantitatively different mechanisms which probably serve two different functions.

In the beginning only qualitative patterns were perceived and studied. Recently, however, Jouvet¹ and others have produced data which show that the sleep states are like rectal temperatures, heart rates and basal metabolism, a biological constant. Thus the two phases, slow wave and paradoxical sleep can be quantitative indexes of the innermost mechanisms of the brain. This has permitted study of the sleep states in relation to quantitative alterations by drugs, by limited brain lesions in relation to data obtained through biochemical analysis. Furthermore, it is now possible to correlate the circadian variation of the sleep states with the circadian biochemical variation in the brain — neurohumoral physiology of the brain.

Neuropharmacology, neurophysiology and histochemical data provide a partial understanding of events involved in paradoxical sleep. Slow wave sleep seems to depend on serotonin containing neurones of the raphe system, while paradoxical sleep seems to depend on noradrenalin containing neurons located in the nucleus locus coeruleum.

The hypothesis that serotonin has a role in the process of sleep is strongly supported by two series of experiments. If synthesis of serotonin is inhibited by p-chlorophenylalanine, then the animal becomes totally insomniac. This state then is made reversible and the animal returns to normal sleep if the immediate precursor of serotonin, 5-hydroxytryptophan, is injected. Serotonin can also be eliminated if the serotonin containing neurons in the raphe system are destroyed. In this case it also leads to total insomnia. Jouvet showed this by the technique of histofluorescence. Thus there appears to exist a three-way correlation between the extent of destruction of the raphe, the decrease of serotonin and the resulting insomnia.

Paradoxical sleep appears to depend upon a "priming" serotonergic mechanism located in the caudal raphe system and upon triggering mechanism located in the nuclei of the locus coeruleum. If these nuclei are destroyed paradoxical sleep is suppressed without alteration of slow wave sleep. When it comes to drugs, paradoxical sleep may be inhibited by at least three categories of drugs. One can increase slow wave sleep by drugs which prevent serotonin destruction, in which case there is total suppression of paradoxical sleep. One can therefore speculate that it is some serotonin metabolite which triggers the onset of the paradoxical sleep mechanism.

Jouvet has also shown that atropine suppresses the final steps of paradoxical sleep. It inhibits muscle tonus, probably inhibits a cholinergic mechanism which in turn triggers off noradrenalin mechanism involved in paradoxical sleep. The successive intervention of serotonergic, cholinergic and noradrenergic mechanisms in the triggering and effecting of paradoxical sleep is strongly implied by the neuropharmacological results. Such a "fact-safe" mechanism must be viewed as contributing to the effectiveness of the organism in that it prevents the intrusion into the waking state of the hallucinogenic processes involved in dreaming.

L.H.N.

References

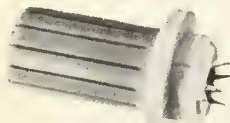
1. Jouvet, M.: Biogenic amines and the states of sleep. *Science*, 163: 32, January 3, 1969.

Studies Of The Renin-Angiotensin System

Within recent years the interrelation between the renin-angiotensin and aldosterone system has been elucidated. The advances have naturally led to the reexamination of the role of renin in a

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variety of human pathologic processes. It now appears that renin is not only involved in normal homeostasis but also is an important factor in the pathogenesis of certain kinds of hypertensive diseases. Renin is synthesized in the vascular pole of the renal glomerulus, the maculae densa of the juxtaglomerular apparatus of the afferent arteriole. One stimulus to renal secretion is "effective blood volume" involving plasma sodium concentration, sodium intake and renal perfusion pressure and actual blood volume.¹

Renin itself is but one part of a complex feedback loop for regulating blood volume and blood pressure. It acts upon a protein in plasma to release angiotensin I an inactive decapeptide. This is then converted to an octapeptide angiotensin II which is both a highly effective pressor agent more so than norepinephrin, but it is also a major stimulus to the secretion of aldosterone even at sub-pressor levels. Aldosterone then leads to reabsorption of sodium by the renal tubule which in turn increases "effective blood volume." This decreases renin secretion and completes the effective feedback loop.

Angiotensin II has a very short half-life. There is a large difference in content of this agent between arterial and venous blood and this suggests that it is the peripheral capillary bed which is in some way involved in its removal. Renin on the other hand has a longer half-life in vivo than angiotensin II and is degraded by the liver.

The stability of the renin angiotensin aldosterone feedback loop is most readily disturbed in normal subjects by change in posture and salt restriction. The lowest renin values are obtained after a period of recumbency. After four hours of normal upright activity renin secretion rises appreciably. In the upright posture the receptors sense an apparently lower "effective blood volume" which then stimulates the secretion of renin. Salt restriction has a similar effect. As a result of an increase in renin secretion circulating angiotensin rises and this in turn stimulates the adrenal cortex to secrete more aldosterone. In response to the aldosterone the renal tubules now resorb more sodium effecting the desired homeostasis.

This interrelationship of the feedback loop makes it possible for us to make a correct diagnosis in two varieties of curable hypertension associated with hyperaldosteronism, renal artery stenosis and an aldosterone secreting tumor of the adrenal gland. In renal artery stenosis because of either lower blood flow perfusion pressure or pulse

pressure the kidney sensor on the affected side interprets a lower "effective blood volume." This action augments renin secretion and is followed by an increase in angiotensin and aldosterone. This variety of hyperaldosteronism is called secondary because it is caused by excess renin secretion.

In functional adrenocortical adenoma on the other hand aldosterone secretion is independent of renin control and is therefore termed primary. Excess aldosterone secretion increases salt and water retention because of an increased effective blood volume and an unimpaired sensing mechanism renin secretion is shut off. Here the interruption in the feedback loop resides in the adrenal tumor. Since it is not under the control of the renin mechanism a decreased level of renin does not decrease the secretion of the aldosterone tumor. The crux of the differential diagnosis between primary and secondary hyperaldosteronism then lies in the finding of a low renin activity in the patient with tumor and a high renin activity in renal in the patient with artery stenosis.

The simple demonstration of an existing renal artery stenosis cannot implicate that lesion as an etiologic factor in a subjects hypertension, because this type of hypertension may not be due to the existing stenosis.² However, renal-vein renin determinations give the clue to a surgical curable case. If there is hypertension, renal artery stenosis and also increased renin production in the affected renal vein, this points to the pathophysiology of the lesion.

A primary adenoma of the adrenal cortex can be a cause of a special hypertensive syndrome (Conn's syndrome). Such patients are easily recognized by striking manifestations of hyperaldosteronism such as hypokalemia, alkalosis and hypernatremia. There can be little doubt that plasma renin determinations are of great value in the evaluation of a hypertensive patient especially in differentiating primary from secondary hyperaldosteronism. Patients with untreated essential hypertension do not have elevated renin activity.

There are several exceptions that are worth bearing in mind. Very high renin levels are found in cirrhosis with ascites and without hypertension, but the hyperaldosteronism here is secondary to a reduced "effective blood volume." The impaired hepatic capacity to metabolize renin might be a contributing factor. An uncommon renal abnormality described by Bartter et al³ is associated with high renin and aldosterone levels but with normal blood pressure. No clear explanation of this

Convalescing . . . but still a long way to go. Anxiety can make it even longer.

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Important Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstated. Severe reactions,

observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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syndrome is yet at hand. Such apparent paradoxes cannot be resolved on the basis of present knowledge.

Now that there are available sensitive and objective methods of measuring the components of the renin-angiotensin system, their widespread use should undoubtedly contribute to the resolution of present clinical physiologic problems and doubtless uncover new problems for further investigation.

L.H.N.

References

1. Haber, E.: Recent developments in pathophysiologic studies of the renin-angiotensin system. *New Eng. J. Med.*, 280: 148, 1969.
2. Holley, K. E., Hunt, J. G., Brown, A. L., Kincaid, O. W. and Shreps, S. G.: Renal artery stenosis clinical pathologic study in normotensive and hypertensive patients. *Am. J. Med.*, 37: 14, 1964.
3. Bartter, F. C., Pronove, P., Gill, Jr., J. R. and MacCardle, R. C.: Hyperplasia of juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis: new syndrome. *Am. J. Med.*, 33: 811, 1967.

Butaperazine (Repoise)

Butaperazine (Repoise-Robins), a phenothiazine of the piperazine group, is offered as a "new potent psychotherapeutic agent for use in the management of chronic schizophrenic patients." Available evidence indicates that the drug is, as claimed, effective against symptoms of schizophrenia, but if the manufacturer's description of it suggests that it is more effective than other phenothiazines, the suggestion is not supported by the evidence.

CLINICAL STUDIES—In both controlled and uncontrolled studies, butaperazine produced symptomatic improvement in patients with chronic schizophrenia. In controlled trials comparing butaperazine with other phenothiazines of the piperazine group, however, no significant differences in effectiveness were found. One trial compared butaperazine with perphenazine (Trilafon) (P. Sharpley et al., *Psychopharmacologia*, 5:209, 1964), another with prochlorperazine (Compazine) (J.-M. Bordelieu et al., *Chemothérapie*, 9:248, 1964), and two others with trifluoperazine (Stelazine) (W. Mandel and P. Evans, *Amer. J. Psychiat.*, 119:70, 1962; M.

P. Bishop et al., *Dis. Nerv. Syst.*, 25:67-1, 1964). In a controlled trial comparing butaperazine with haloperidol (Haldol), a butyrophenone the two drugs were about equally effective (H. Warnes et al., *Laval Med.*, 37:143, 1966).

There have been no reports of controlled trials comparing butaperazine with phenothiazines other than those in the piperazine group. A recent controlled study, like other studies, has failed to confirm the clinical impression that the piperazine phenothiazines are more effective than other types of phenothiazine drugs in apathetic or retarded patients (S. C. Goldberg et al., *Arch. Gen. Psychiat.*, 16:107, 1967).

ADVERSE EFFECTS AND PRECAUTIONS—Tremor and other extrapyramidal side effects have been frequent with butaperazine. In the studies cited above, they occurred at least as often, and in two studies more often, with butaperazine than with the other piperazine phenothiazines, and required either reduction of dosage or administration of antiparkinsonism drugs. Other side effects included drowsiness and postural hypotension, with unsteadiness or, rarely, syncope. No cases of agranulocytosis or jaundice have been reported with butaperazine, but as the manufacturer states, all of the side effects of the phenothiazines may occur.

DOSAGE—The manufacturer suggests initial oral doses of 5 to 10 mg three times a day, with increases of 5 to 10 mg every few days until a maximum response is achieved or side effects are excessively disturbing. Total daily dosage should not exceed 100 mg.

CONCLUSION—Butaperazine is another in the long list of drugs effective against symptoms of schizophrenia. Available evidence does not demonstrate any advantages over older drugs with which there has been greater experience. For this reason and because new drugs always carry the risk that new and possibly serious adverse effects will appear with longer use, Medical Letter consultants see no reason to choose butaperazine for the treatment of schizophrenia.

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Foreword

A NEW MEDICAL SCHOOL FOR CONNECTICUT

The School of Medicine of the University of Connecticut is indebted to the Editor, Dr. Louis H. Nahum, for offering to devote one special issue of *Connecticut Medicine* to the new school. We are grateful for this formal introduction to the medical profession of the State. The articles in this issue are from the faculty of the new school. One describes the undergraduate medical education program and another is concerned with the organization of the departments concerned with pediatrics and medicine. These are included because the programs in these two areas at the University of Connecticut depart from the traditional pattern.

Although an interest in developing a new State-supported School of Medicine had existed for many years, the idea started to become a reality in 1960 when the University of Connecticut received a grant from the Kellogg Foundation to start a two-year school of basic science. The State Legislature demonstrated its backing in 1961 by authorizing the expenditure of two million dollars to start a Medical and a Dental School and by authorizing the Governor to appoint a commission to choose a site in Greater Hartford. By 1963 the concept had grown to include four-year Schools of Medicine and Dental Medicine. In that year Doctors Lyman M. Stowe and Lewis Fox were appointed as the first Deans of the two Schools. Each of the Deans appointed two faculty members to assist with the planning. Following the sudden and unexpected death of Dr. Stowe in June of 1965, Dr. John W. Patterson assumed the responsibilities as Dean of Medicine. Before and after this time, the plans for a Health Center in Farmington were developed. The various programs are now being initiated.

The main building of the Health Center is designed to accommodate Schools of Medicine and Dental Medicine each having starting classes of 48 students, and a University Hospital of 200 beds with supporting ambulatory clinics. This facility is more than one million square feet in size and incorporates a number of new ideas. Among these are: home-base multidiscipline laboratories for students, enabling the faculty to come to the students rather than having students go from department of department; circular patient care units so that patients' anxieties regarding the availability of help are relieved by maintaining visual contact between patient beds and nursing stations; decentralized ambulatory clinics which avoid congestion by providing small waiting areas near the point of patient care and have receptionists who can make appointments and accept payment on bills; numerous technical developments such as Cyberail for materials transport in the hospital and clinics, closed circuit television for communication, and a computer center for administrative, research, and patient care activities. These facilities are now under construction and will be occupied as various areas are completed during the next three years. In the meantime, other facilities are being used temporarily.

The hospitals in the Hartford area are considered to be outstanding. Affiliation arrangements for educational programs have been made with Hartford, Saint Francis, Mount Sinai, New Britain, and Middlesex Hospitals. Others are under consideration. The University assumed the responsibility for the operation of McCook Hospital on July 1, 1967. The responsibility for professional staffing

of the Veterans Administration Hospital in Newington is being transferred from the Advisory Committee of Hartford Hospital to the Dean's Committee of the University. The School of Medicine is thus responsible for the professional activities in these two hospitals. There are approximately 350 beds for acute patient care, and an additional 60 beds for convalescent patient care.

Faculty appointments are proceeding in a regular manner. Six out of a total of eight basic science department chairmen have been appointed and are working in the Hartford area. Eight of the nine medical clinical department heads have been appointed. Three are now active in Hartford, four will be arriving during the next school year, and two in the following year. During the present year, the School of Medicine faculty is made up of approximately 60 individuals. They are actively engaged in education, research, and patient care.

The educational programs are of four different types: those leading to an M.D. and D.M.D. degree, graduate professional programs for interns and residents, continuing education programs for physicians and dentists, and Ph.D. programs for medical science. All of these are being started.

The program leading to the M.D. and D.M.D. degree was started in September, 1968, with the admission of the first class of 30 medical and 18 dental students. A class of similar size has been selected for the fall of 1969. It is anticipated that the student facilities in the main building will be ready by the summer of 1970, and it will then be possible to admit a total of 96 students in the combined medical and dental freshman class.

An integrated interuship and residency program has been arranged for the Veterans Hospital in Newington and the McCook Hospital. Accreditation has now been received for an internship program and for residency programs in Medicine, Pediatrics, Pathology and Urology. Twenty-five interns and residents will be involved in the program starting July 1, 1969.

Programs in continuing education are being developed in conjunction with affiliated hospitals. These are based on the concept that full-time chiefs-of-service can play an important role in continuing education and serve as a bridge between the Health Center and the community hospital. At the present time, eight full-time chiefs-of-service have been appointed at affiliated hospitals and an active search is continuing for five others.

The Ph.D. programs for medical scientists are intimately related to the research activities of the faculty. Although there were a few active research projects before 1968-69, most of the faculty arrived and started their research during that year. This resulted in the attraction of over one and a half million dollars of research support for projects being conducted during the current year. Graduate students are gradually being attracted to the departments with the first candidate for a Ph.D. degree scheduled to complete all the requirements by June 1969.

Thus, a new medical school for Connecticut is no longer a dream but reality. The construction program is under contract, the nucleus of an active faculty group is on hand, and programs of education at all levels are now in progress. In a few years, graduates of these programs will be taking their place in the health care activities of this State.

JOHN W. PATTERSON, M.D., *Dean*
Guest Editor

Pituitary Regulation by the Hypothalamus: Functions of the Median Eminence Gland

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The median eminence of the hypothalamus forms a glandular part of the brain, which has as its function the regulation of the anterior pituitary gland.

That the anterior pituitary gland is controlled by the brain has been suspected for a long time. Case reports of pituitary failure in patients with hypothalamic disease have appeared with regularity since Froehlich's account of adiposigenital dystrophy in 1901, and, even before this¹ anatomic evidence of neural control of gonadotropic function was well recognized in certain animals. Several species of animals such as rabbits do not ovulate unless copulation occurs. Only at the time when successful insemination can occur does ovulation take place. In other animals, there is an endogenous neural rhythm for ovulation. Through hormonal effects on the brain, behavioral change is made to correlate with ovulation, so that the female will accept the male only when there is an egg ready. These seem to be the two principal methods in mammals by which deposition of semen is made to correlate with readiness of the ovum. The human being is exceptional in this regard, because the

relation between sexual receptivity and ovulation seems to be more informal. More recent advances using specific methods for hormone analysis reveal that all of the hormones of the anterior pituitary are affected by brain function. For example, both psychic and physical stress induce ACTH discharge, and growth hormone release. In recent years the operation of pituitary-stalk section has been introduced for the management of some diseases, particularly diabetes, and a number of endocrine deficits follow this procedure (1, 2).

Two illustrations from the literature indicate some consequences of section of the pituitary stalk in man (Figure 1). Dugger and his colleagues evaluated the effect of pituitary stalk section in women on the course of carcinoma of the breast.¹ Coincidentally, they studied thyrotropic and other pituitary tropic functions. Preoperative uptake of radioactive iodine ranged from 5 to 40 per cent. When the preoperative uptake was in the normal range to begin with, it was lowered by stalk section. It has been uniformly found that a degree of thyroid insufficiency follows section of the stalk in the human subject, but it is not so complete as that seen after hypophysectomy. Similar observations have been made in rabbits and in other laboratory animals³ (Figure 2).

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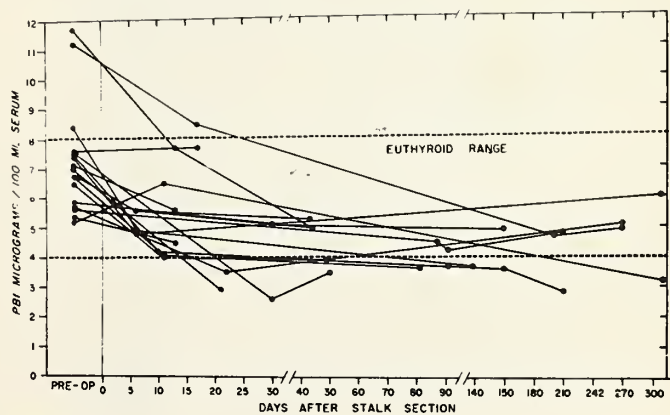
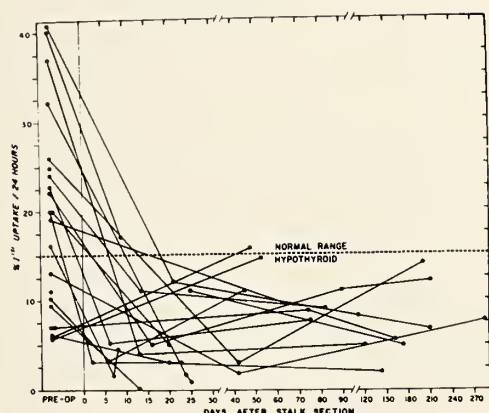


Figure 1

- A. The ¹³¹I uptake in 19 patients before transection of the stalk and at various times after operation.
B. The PBI in 17 patients before transection of the stalk and at various times after operation. The euthyroid range lies between the two horizontal dashed lines. (Dugger, VanWyk and Newsome, J. Neurosurg. 19: 589, 1963).

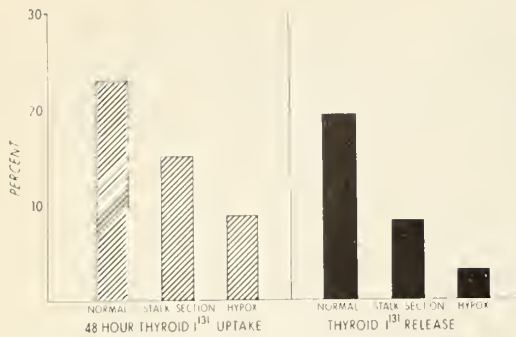


Figure 2

Effect of section of pituitary stalk in the rabbit on thyroid function.

It is hard to interpret stalk-section experiments as specific effects, however, because in man 90 per cent of the pituitary gland is infarcted by section of the stalk. This is due to the fact that almost all the blood vessels that supply the anterior pituitary gland pass via the stalk.⁴ But collateral evidence can be cited to show that the effect is due to loss of specific neurohumoral control and not to vascular insufficiency alone. The observations of Ehni and Eckles² on the effect of stalk section in producing lactation in women (Figure 3) are impossible



Figure 3

Copious lactation from the remaining breast following permanent interruption of the pituitary stalk. (Ehni and Eckles, *J. Neurosurg.* 16: 628, 1959).

to interpret except in the light of current ideas about neurohumoral control of the pituitary gland.⁵ This pituitary "denervation" syndrome is analogous to that seen in a number of clinical states in which the pituitary stalk has been damaged — for example, in Boeck's sarcoid of the hypothalamus, which may cause lactation. Large doses of chlorpromazine or of reserpine, both of which act on the hypothalamus, may also cause lactation. The syndrome of nonpuerperal galactorrhea is probably caused in most cases by a similar mechanism. The curious situation exists in stalk-sectioned human patients that the secretion of all the other tropic hormones is inhibited but that of prolactin seems to be increased despite the fact that these pituitary glands show very marked regressive changes anatomically. These are very small glands, and yet they are capable of secreting large amounts of prolactin.

To understand these observations, one must examine the anatomy and physiology of the hypothalamic-pituitary unit (Figure 4). The median eminence is the central portion of the base of the hypothalamus and forms a structure that has been modified so that humoral substances secreted by

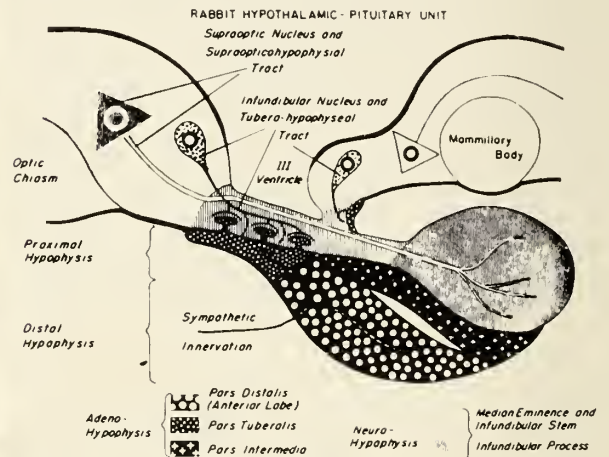


Figure 4

Semidiagrammatic Sagittal Section of the Rabbit Brain, Demonstrating the Anatomic Relation between the Base of the Hypothalamus and the Pituitary Gland (Adapted from Spatz).

Unlike conventional diagrams, this figure emphasizes two distinct neurovascular transmission systems. One system, best known, is the supraopticohypophysial tract, which arises in the supraoptic nuclei and terminates in relation to blood vessels of the neural lobe. The other system, whose neurons probably arise in the tuberal region of the hypothalamus, terminates in relation to the blood vessels of the median eminence. In view of its postulated role in neurohumoral regulation of anterior lobe function this region of the brain may be considered the "median eminence gland" (Reichlin, 3).



Figure 5

Base of a Rat Brain, Showing the Pituitary Blood Supply Perfused with India Ink.

The boundaries of the hypothalamus viewed from beneath are the optic chiasm (anteriorly) and the mammillary bodies (posteriorly, and covered by the pituitary gland). Laterally are the temporal lobes. The primary plexus of the hypophysial-portal blood supply ramifies in the substance of the median eminence of the hypothalamus.

nerve endings in this region can be transmitted by way of blood vessels to the anterior pituitary gland.

The median eminence is innervated by a number of very small fibers that are located around the base of the hypothalamus. The nerves end in relation to perivascular capillary spaces and the blood from these capillaries is delivered finally to the anterior lobe by the hypophysial-portal circulation. The arterial blood, which perfuses the median eminence capillaries, is enriched by neurohumors, called releasing factors secreted by these nerve endings.

This system can be visualized in animals by perfusion of the vessels with ink (Figure 5). In rats the portal-vessel capillary plexus consists of loops that dip into the substance of the median eminence and neural stalk. There is some variation in the morphology of the system among species. In man these vessels have very thick muscular walls undoubtedly capable of reflex vasoconstriction. It has

been postulated that in Sheehan's syndrome reflex spasm of these portal vessels is followed by infarction of the pituitary gland. In man, 90 per cent of the blood that reaches the pituitary gland first perfuses the stalk median eminence vascular bed.

Viewed by electron microscopy, the median eminence is seen to be made up of a mass of packed nerve endings, capillaries and perivascular spaces (Figure 6). These clubbed nerve endings contain small vesicles, which are thought now to contain neurohumoral material. The vesicles are emptied of these pre-formed neurohumors, which diffuse through plasma membrane, perivascular space, capillary basement membrane and capillary endothelial wall and then enter the portal vessel bloodstream.

Many classic experiments could be cited to support the view that this region of the brain is uniquely capable of regulating anterior pituitary function. Transplants of the pituitary gland under

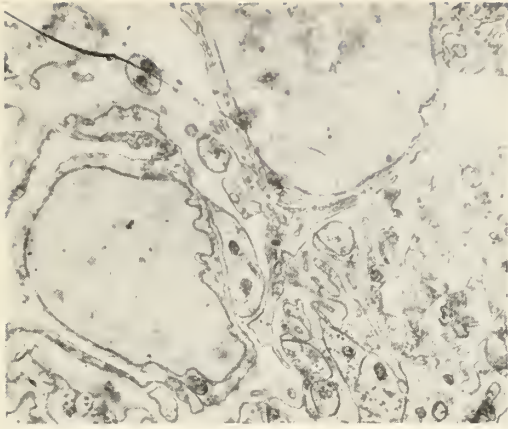
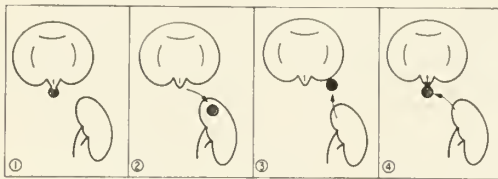


Figure 6

Electron micrograph of hamster median eminence. The median eminence is made up of densely packed nerve endings distributed in relation to the perivascular space of the primary portal capillaries in a schema resembling in principle the distribution of nerve endings in the neurohypophysis. The nerve endings shown here in cross-section profiles contain a variety of vesicles, both large and small, and of differing electron density which are thought to contain neurosecretions. Mitochondria are also found. Note that nerves end in close relation to a basement membrane. The path of secretion is from nerve endings, through axon basement membrane, perivascular connective tissue space, capillary basement membrane, and finally endothelium. This is the characteristic arrangement of glandular cells throughout the endocrine system. (Courtesy Dr. Karl M. Knigge).

the median eminence (Figure 7), or into the hypothalamus itself (Figure 8) supports pituitary function whereas transplants elsewhere are without effect. On this basis Dr. Bela Halasz, a Hungarian physiologist, has postulated that the ventral hypothalamus is hypophysiotropic. By that he means that this portion of the brain is specialized to



ESTRUS CYCLES	100 %	0	0	93 %
PREGNANCY	100 %			50 %
OVARIAN WT mg/100 gm BW	27	6.1	4.3	16
THYROID I ¹³¹ UPTAKE (24 hr)	7 %	1.2 %	33 %	3 %
ADRENAL WT mg/100 gm BW	51	2.4	2.8	54

SUMMARY OF PITUITARY RE-TRANSPLANTATION STUDIES (NIKITOVITCH-WINER AND EVERETT)

Figure 7

Specificity of the Median Eminence as the Source of Blood Supply to the Anterior Pituitary Gland (Reproduced from Bryson and Reichlin, 6, with Permission of the Publisher) (Adapted from Nikitovitch-Winer and Everett, 5).

Pituitary tissue retransplanted (and thus twice insulted) is still capable of restoring toward normal gonadal, thyroid and adrenal function in other sites (kidney, temporal lobe of the brain) is reduced to the level of hypophysectomized animals.

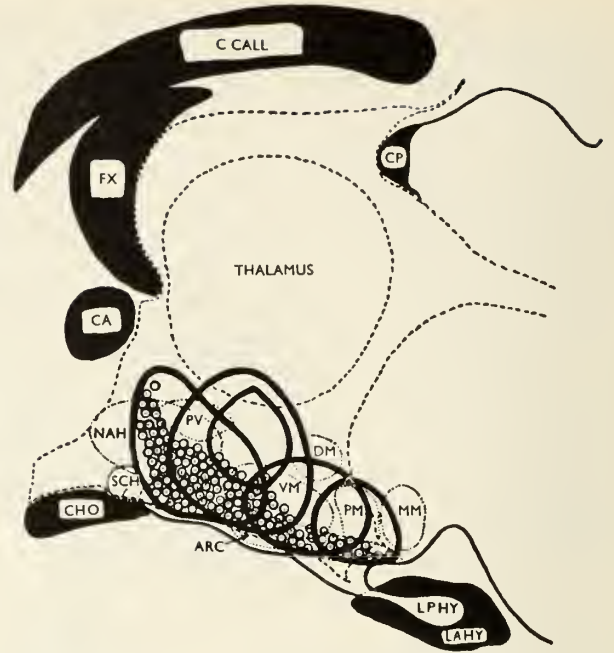


Figure 8

Diagrammed here is the "hypophysiotropic area" of the hypothalamus. Pituitaries transplanted into various regions of the brain show morphological differentiation, and some tropic function. This observation indicates that there is a "field" of hypophysiotropic neurons within the hypothalamus. These probably correspond to the cell bodies of the tracts to the median eminence.

---, Outline of the third ventricle; ····, midsagittal projection of main hypothalamic nuclei; —, borders of five relatively midline pituitary grafts; PAS-positive basophils; ARC, arcuate nucleus; CA, anterior commissure; C CALL, corpus callosum; CHO, optic chiasma; CP, posterior commissure; DM, dorsomedial nucleus; FX, fornix; LAHY, anterior lobe of hypophysis; LPHY, posterior lobe of hypophysis; MM, medial mammillary nucleus; NAH, anterior hypothalamic nucleus; PM, premammillary nucleus; PV, paraventricular nucleus; SCH, supra-chiasmatic nucleus; VM, ventromedial nucleus (Halasz, Pupp and Uhlarik, *J. Endocrinol.* 25: 147, 1962).

secrete material that causes differentiation and increased pituitary function. These probably are the same regions that contain the cell bodies of origin of the tuberal-hypophysiotropic tracts, which ultimately end in the median eminence.

If the median eminence is indeed a neuroendocrine organ for the regulation of anterior pituitary function, it should be possible to cause deficits by means of destructive lesions, to induce secretion by electric stimulation and to isolate neurohumoral transmitters capable of altering pituitary function. This theoretical model of hypothalamic-pituitary control, attributable in large measure to the work of G. W. Harris and J. D. Green, has inspired an enormous amount of re-

search into the regulation of all the pituitary tropic hormones.

In this presentation the endocrine function of the median eminence will be further illustrated with some recent studies of growth hormone regulation. We are in a particularly fortunate position to analyze control mechanisms for secretion of growth hormone because this pituitary hormone is now readily measurable in the blood. Most previous neuroendocrine studies have depended upon secondary changes in target organ function or appearance. Glick et al (8) are responsible for the demonstration by immunochemical assay that the growth hormone regulating system is extremely labile. It used to be thought, and not so very long ago, that growth hormone was involved primarily with growth regulation; since growth follows a long time course, it was assumed that variations in growth hormone secretion must also be rather torpid — greater in the young and gradually disappearing during aging. All this seems to be wrong, except for the fetus and newborn infant. Beyond the early weeks of life growth hormone levels in the fasting state are virtually the same at all ages. There does not appear to be an adolescent peak, nor does there appear to be a senium for growth hormone secretion. On the other hand, relatively trivial activities of the day may be associated with marked changes in growth hormone secretion. For example, Rabkin has recently found that the exer-

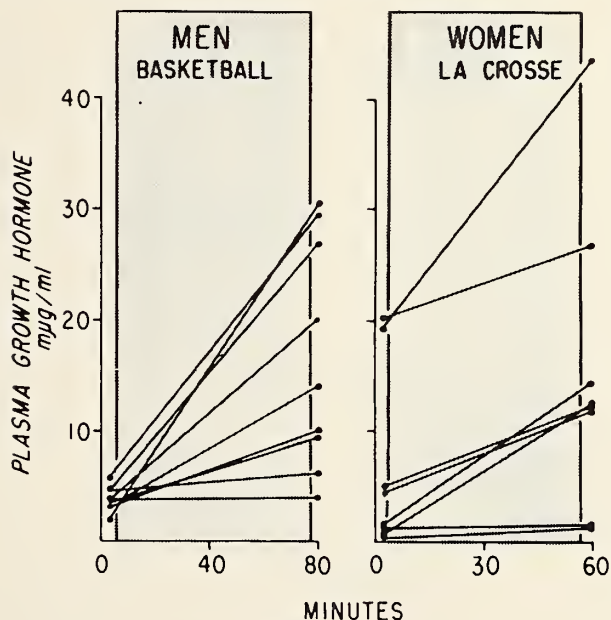


Figure 9

The effect of competitive exercise on plasma GH is illustrated in young men playing basketball and young women playing lacrosse (Schalch, J. Lab. Clin. Med. 69: 256, 1967).

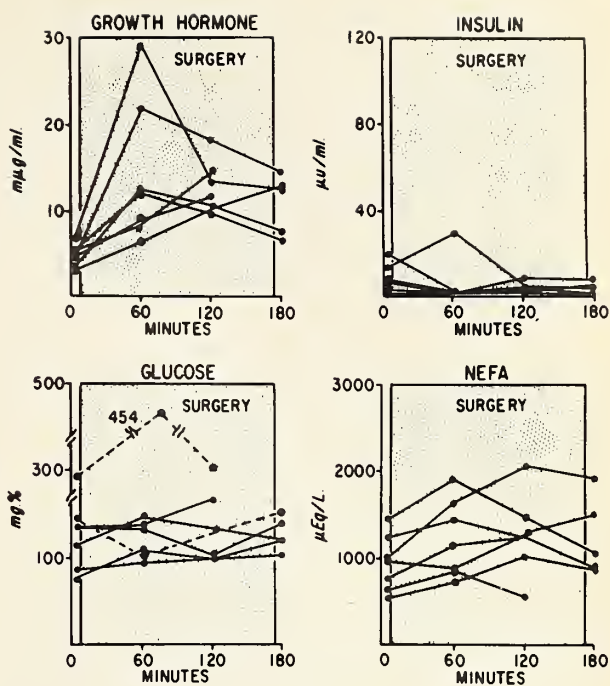


Figure 10

Changes in plasma growth hormone, insulin, glucose and NEFA during major surgery. The plasma glucose values for the 2 patients who received intravenous glucose solution during surgery are represented by the dashed lines. (Schalch, D. S., J. Lab. Clin. Med. 69: 256, 1967).

cise of getting out of bed in the morning (in women) will raise the growth hormone level. Dr. Don Schalch at the University of Rochester studied growth hormone levels in medical house officers playing basketball (Figure 9). In almost everyone, after an hour of basketball, the growth hormone levels were raised.

Similarly, the stress of surgery is accompanied by a rise in growth hormone level as first shown by Glick and collaborators and confirmed by Schalch (Figure 10). Conditioned stress in the human will also increase GH release (Figure 11).

It is important to point out that there are fluctuations in relation to meals also. Immediately after a meal the growth hormone levels fall and then rise as blood sugar falls. The cyclical changes of the levels in man may be responsible in part for the cyclical variations in substrate utilization in peripheral muscle that have been demonstrated by Zierler and Rabinowitz (9).

One of the most interesting discoveries resulting from the use of radioimmunoassay of growth hormone was that of Roth and his collaborators, who found that hypoglycemia triggered the release of growth hormone in man. After injection of insulin blood sugar levels fall, and growth hormone levels

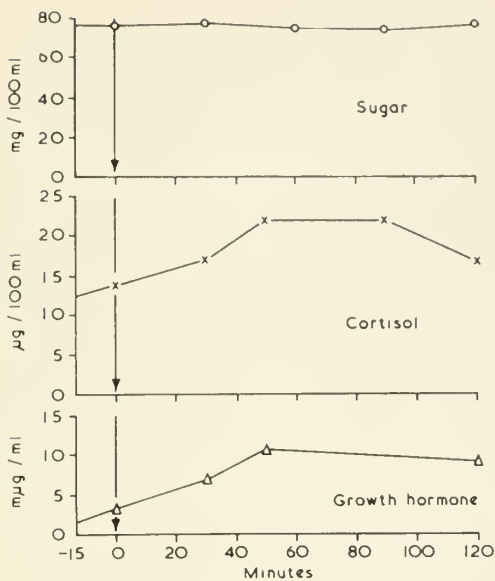


Figure 11

The effect of an emotional stress on plasma cortisol and growth hormone. Saline was injected (vertical arrow) into a volunteer member of the medical staff expecting a "massive dose" of insulin and subsequent hypoglycemic symptoms. Significant rises in the levels of plasma cortisol and of plasma growth hormone followed injection without changes in the level of plasma sugar. (Greenwood and Landon, *J. Clin. Path* 19: 284, 1966).

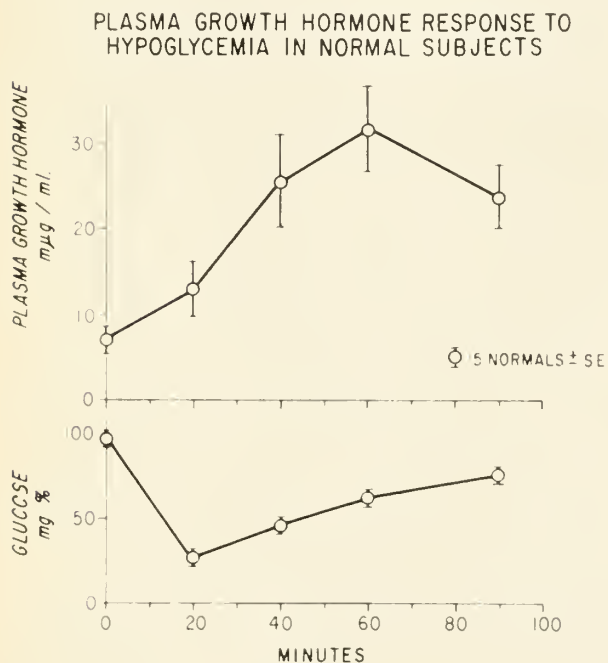


Figure 12

Insulin-induced hypoglycemia is a marked and predictably effective stimulus of GH hypersecretion as shown in this experiment on 15 normal individuals (Schalch, 1966, unpublished).

rise progressively and then return toward normal. The response in man is highly reproducible and has proved to be a valuable tool for evaluation of pituitary failure (Figure 12).

The response to hypoglycemia provided the key to our experimental study of the mechanism by which the brain controls growth hormone secretion. Working in collaboration with Drs. Robert L. Abrams and Santander Blanco at the University of Rochester, and with Drs. Mary L. Parker and William H. Daughaday of St. Louis, we studied the effect of hypothalamic lesions on reflex discharge of growth hormone in the monkey (10). The monkey was chosen for this experiment because monkey growth hormone is immunologically crossreactive with human growth hormone.

To do the experiment, the monkey must first be caught and placed in a restraining chair. Blood is taken from a previously placed indwelling cannula to avoid the psychic trauma of venipuncture: While the animal sits resting in its chair recovering from the chase and capture, growth hormone levels gradually fall (Figure 13). We think this is because

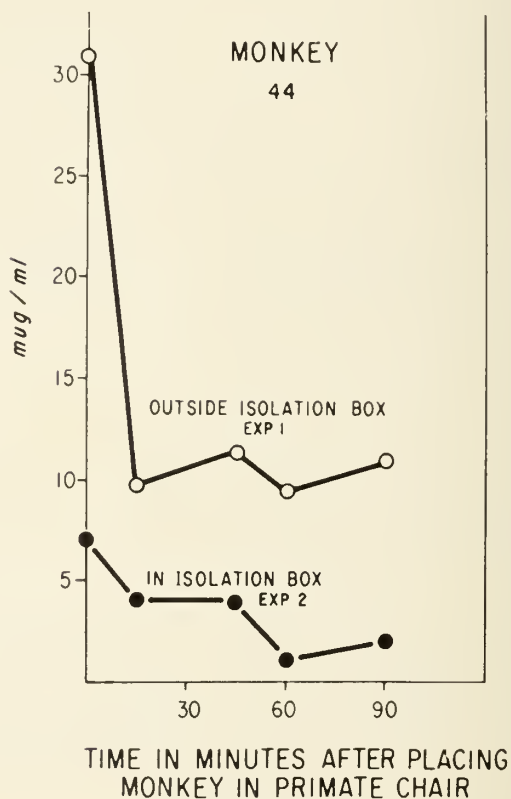


Figure 13

Plasma GH levels in a squirrel monkey during recovery from capture and initial handling. Initial high levels are uniformly observed. These gradually return to normal (Gross, Schalch and Reichlin, unpublished).

the monkey is recovering from the stress of capture and exercise. Knobil (11) reported that the rhesus monkey behaves similarly. As trivial a stimulus as the ringing of a bell or slamming of a door will cause a dramatic rise in growth hormone level. Because of this nonspecific reaction to stress, it is extremely important to guard the monkey against extraneous stimuli. All our own work has been done after a period of stabilization in an isolation booth to allow the monkey to become accustomed to his new environment.

The growth hormone response to insulin-induced hypoglycemia is identical in the monkey and in man (Figure 14). Once it has been determined that one can reproducibly induce growth hormone discharge by injection of insulin in the monkey, the next step was to see what structure was responsible. Various regions of the brain, in the base and elsewhere, were destroyed under stereotaxic control. The anterior median eminence was chosen as a particular target because, in rats, destruction here causes the animal to grow poorly. Certain ventral hypothalamic lesions were found to abolish growth hormone discharge, whereas others were without effect (Figure 15). Lesions that did not produce "growth hormone block" were located in the mamillary body and the preoptic area, in the optic chiasm and in the anterior lobe. A small lesion on one side of the median eminence was

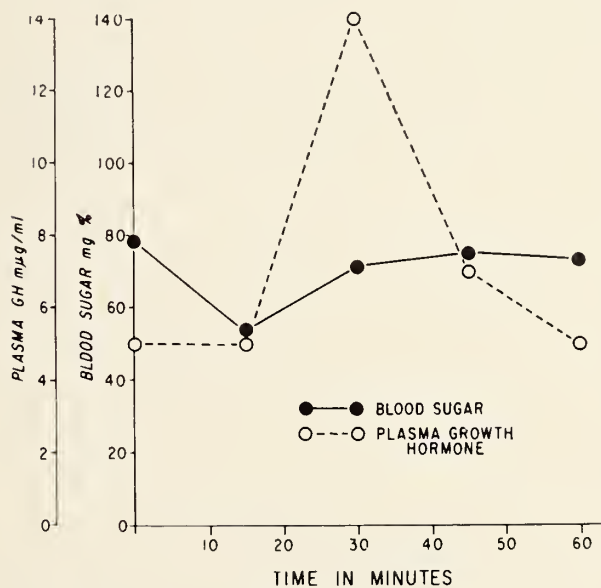


Figure 14

Blood Glucose and Plasma Growth Hormone Response to Hypoglycemia in the Squirrel Monkey.

As in man, insulin (0.15 unit per kilogram of body weight) lowered the blood glucose level and stimulated the release of growth hormone (Abrams et al, *Endocrinology* 78: 605, 1966).

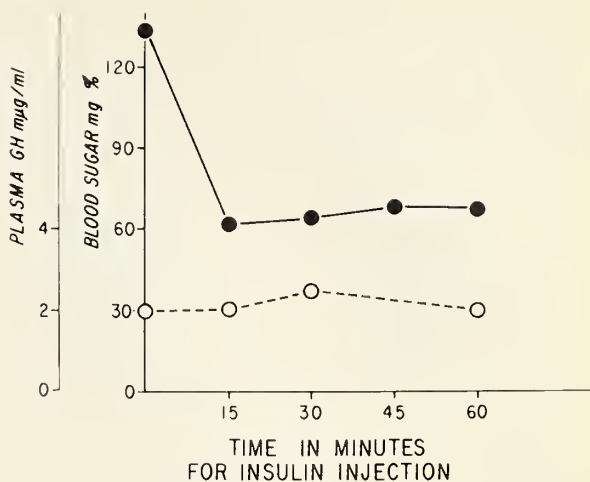


Figure 15

Blood Glucose and Plasma Growth Hormone Response to Hypoglycemia in a Squirrel Monkey with an Electrolytic Lesion in the Anterior Median Eminence.

In this animal growth hormone levels failed to rise despite the fact that blood glucose concentrations fell as much as in the normal animal. Animals of this type have been described as manifesting growth hormone blockade. The solid circles represent blood glucose and the open circles plasma growth hormone. (Abrams, et al, *Endocrinology* 78: 605, 1966).

also without effect on growth hormone response. Lesions that blocked the response were clustered in the base of the hypothalamus in the median eminence region (Figure 16). This work indicated that the base of the hypothalamus was involved in reflex growth hormone discharge in response to hypoglycemia. It will be recalled that Roth and his collaborators studied a patient with stalk section who also had a blockade of the growth hormone response to hypoglycemia. Recently, Greenwood's group reported similar blockade of growth hormone response in certain patients with hypothalamic disease (12). There appears to be little doubt that the growth hormone response to hypoglycemia involves a neural mechanism in both man and laboratory animals.

Another curious finding in the study by Abrams and his collaborators was that fasting growth hormone levels were not depressed by lesions. Fasting levels varied widely, but in animals with these lesions they were not significantly different from controls. This was true for Roth's patient with stalk section as well, and suggests that the "setting" of the basal level of growth hormone secretion may be an autonomous pituitary function but that reflex responses involve the brain. Since normal persons are exposed to varying stimulation of growth hormone secretion through the ordinary day's activity and by meals, it can be assumed

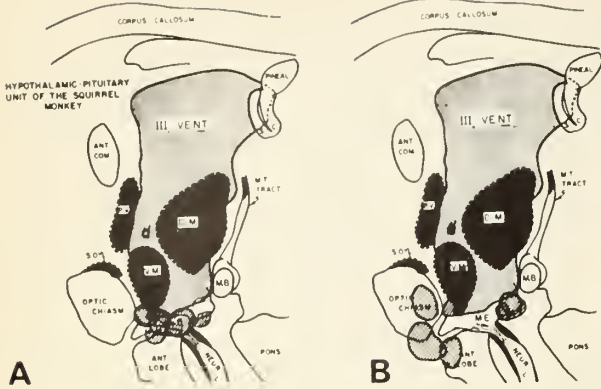


Figure 16

Plotted on a semischematic diagram of the diencephalon-pituitary region of the squirrel monkey in heavy enclosed hatched lines is the position of lesions which blocked reflex GH release (A) and those which did not (B). GH "block" was produced by lesions involving anterior median eminence, the junction of the median eminence and the pituitary stalk; normal GH responses were noted after destruction of the posterior median eminence, anterior hypothalamus, and with lesions in the optic chiasm and anterior lobe of the pituitary. One animal (not illustrated) had normal GH responsiveness despite a small unilateral lesion of the median eminence. Abbreviations: ant. com, anterior commissure; D.M., dorso-medial nucleus; M.B., mammillary body; M.E., median eminence; M.T. tract, mammillothalamic tract; Neur. L., neural lobe; P.V., paraventricular nucleus; S.C., subcommissural organ; S.O., supraoptic nucleus; III vent., third ventricle. (Abrams, Parker, Blanco, Reichlin and Daughaday, *Endocrinology* 78: 605, 1966).

that hypothalamic destruction lowers 24-hour total secretion without affecting so-called basal resting levels.

If the median eminence is a gland, it ought to be possible to find its hormone and to show that the hormones of that gland affect the anterior pituitary gland. A number of workers have demonstrated growth hormone releasing effects from hypothalamic extracts using rat systems of several types.

We have found, as Knobil and Katz have, that injection of extract of sheep median eminence raises growth hormone levels. Since the anesthetized squirrel monkey apparently does not respond to injections of vasopressin, even in large amounts, it appears likely that the effects produced by hypothalamic extracts are not due to the vasopressin contaminant but may be due to the somatotrophin-releasing factor. There is still controversy among investigators in this field as to whether or not SRF has been demonstrated in rats, principally because results obtained by bioassay differ from those obtained by immunoassay. This question was not

resolved by a recent workshop conference sponsored by the NIH (Meites, 1969).

Since the ventral median eminence is made up chiefly of nerve endings, it ought to respond to electric stimulation as other nerves do. Dr. Monroe Gross in our group has worked on this problem. A number of electrode placements have been made in squirrel monkeys, the electric stimulation of which causes a rise in plasma growth hormone (Figure 17). Full histologic analysis of this material has not been completed.

If one takes all the accumulating evidence together (although I must say that there is a great deal more work to do) it may be postulated that the reflex response to hypoglycemia (and probably to the other things that affect growth hormone) involves the median eminence; this pathway is electrically excitable and is mediated through a growth hormone — releasing neurohumor. This region contains a glucoreceptor or is affected by adjacent glucoreceptors.

The significance of this GH discharge must be considered. In a teleologic way, the destructive or catabolic effects of the adrenal steroids, which are also released during stress, are materially influenced by growth hormone. The semistarved animal in negative nitrogen balance will have a much decreased negative nitrogen balance if given growth hormone. Growth hormone is anticatabolic and conserves protein stores, and it may play an as yet undefined part in the maintenance of health in the adult.

It is possible to describe in similar detail the experiments of many workers on the regulations of TSH, ACTH and the gonadotropins. The feedback

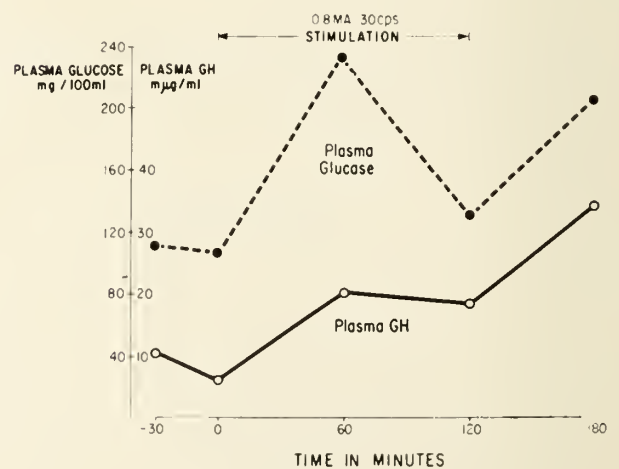


Figure 17

Electrical stimulation of the anterior-ventral median eminence caused a rise in GH level in this chair-adapted monkey.

homeostatic regulation of the pituitary gland by target gland hormones has not been repudiated by the neuroendocrine concept, but the locus of feedback control has now been better defined. In some target systems hormones act principally on the pituitary gland, and in others on the hypothalamus. With respect to the thyroid gland the principal feedback is to the pituitary gland; the hypothalamus seems to act by determining the "set point" of the pituitary-thyroid axis. There may be a feedback to the brain too, but data on this point are controversial. Regarding ACTH control, it is highly probable that the major feedback is to the brain. Almost all the data indicate that both the hypothalamus and certain other brain structures are hydrocortisone targets. Feedback control of the gonadotropins is primarily directed to the brain, but certain effects of the sex hormones directly on the pituitary gland itself may, in well specified circumstances, actually work contrary to the effect of the hormone on the brain. The problem of growth-hormone feedback is still obscure except for glucose regulation, as discussed before. Amino acid perfusions raise growth hormone levels but only in large doses, which may not be relevant to normal function, and growth hormone itself may inhibit GH secretion. Beyond that, the factors that determine the "set point" for regulation of growth hormone are unknown.

Finally, the current status of the other hypophysiotropic hormones can be summarized in a few words (Table 1). (See Schally et al., 1969 for review). All these materials are truly hypophysiotropic. They are not only "releasing factors" but also tropic factors. Median eminence extracts will maintain the morphology, differentiation and function of pituitary grafts. The releasing factors stimulate function, growth and probably hormone synthesis. But they are called releasing factors because of the historical fact that it is their releasing activity that was first detected and that permitted the development of useful assays. The best known of all is the corticotropin-releasing factor. The term was coined by Saffran and Schally, who demonstrated in pituitary tissue cultures that the addition of hypo-

thalamic extract caused a discharge of ACTH into the medium. Subsequently, thyrotropin releasing factor was identified. It is definitely not TSH. It is effective in extraordinarily high dilution and it is found in extremely small amounts in tissue. For example, from 50 kg of sheep hypothalamus, Guillemin obtained only about 10 mg of material. Similarly, luteinizing-hormone releasing factor has been identified. Extracts of median eminence given to rats will raise plasma luteinizing hormone levels, or, if injected directly into the pituitary gland, will trigger ovulation in rats and rabbits. FSH-releasing factors have also been demonstrated in rats.

The subject of prolactin regulation has been saved for the last to explain the strange phenomenon of lactation that develops in women after section of the pituitary stalk. All the releasing factors described above stimulate positively: in their absence pituitary function is decreased, and in their presence pituitary function is accelerated. Prolactin secretion is unique in this regard. It is the only anterior pituitary hormone that is secreted in increased amounts when the gland is divorced from the hypothalamus. When it is transplanted away from the hypothalamus, or placed in organ incubates, prolactin secretion is enhanced. On the basis of the latter finding and the fact that addition of hypothalamic extracts to pituitary incubates inhibits prolactin secretion, Dr. Meites introduced the term prolactin-inhibiting factor. It appears probable that many of the cases of nonpuerperal galactorrhea are due to a deficiency of the prolactin-inhibiting factor, and that the lactation observed after chlorpromazine treatment is due to inhibition of the release of the prolactin inhibiting factor.

The median eminence may be viewed as a neuroendocrine organ, the specific function of which is control of the anterior pituitary gland. The amount of control exerted is somewhat variable from one tropic system to another. For some systems, as for growth hormone, there is a reasonable amount of autonomy; for TSH regulation, there is somewhat less. Gonadotropic hormone secretion is almost totally dependent upon hypothalamic influences. For all systems, it has become clear that the hypothalamus occupies the crucial role in integrating homeostatic and behavioral responses to alterations in the internal and external environment.

TABLE 1

HYPOPHYSIOTROPIC HORMONES OF THE MEDIAN EMINENCE

- Corticotropin Releasing Factor (CRF)
- Thyrotropin Releasing Factor (TRF)
- Somatotropin Releasing Factor (SRF)
- Follicle Stimulating Hormone Releasing Factor (FRF)
- Luteinizing Hormone Releasing Factor (LRF)
- Prolactin Inhibiting Factor (PIF)
- Melanocyte Stimulating Hormone Inhibiting Factor (MSH-IF)

References

1. Dugger, G. S.; VanWyk, J. J. and Newsome, J. F., Effect of pituitary-stalk section on thyroid function and gonadotropic hormone excretion in women with mammary carcinoma. *J. Neurosurg.* 19: 589-593, 1962.

2. Ehni, G. and Eckles, N. E., Interruption of the pituitary stalk in patient with mammary cancer. *J. Neurosurg.* 16: 628-651, 1959.
3. Reichlin, S., *Neuroendocrinology*. New Eng. J. Med. 269: 1182-1191, 1246-1250, 1296-1303, 1963.
4. Adams, J. H., Daniel, P. M. and Prichard, M. M. L., Some effects of transection of pituitary stalk. *Brit. Med. J.* 2: 1619-1625, 1964.
5. Nikitovitch-Winer, M. and Everett, J. W., Functional restitution of pituitary grafts re-transplanted from kidney to median eminence. *Endocrinology* 63: 916-930, 1958.
6. Bryson, M. F. and Reichlin, S., *Pediat. Clin. North America*, 13: 423-436, 1966.
7. Halasz, B., Pupp, L., Uhlarik, S., and Tima, L., Further studies on hormone secretion of anterior pituitary transplanted into hypophysiotrophic area of rat hypothalamus. *Endocrinology* 77: 343-355, 1965.
8. Glick, S. M., Roth, J., Yalow, R. S. and Berson, S. A.: Regulation of growth hormone secretion. *Rec. Progr. Hormone Res.* 21: 241-270, 1965.
9. Zierler, K. L. and Rabinowitz, D., Roles of insulin and growth hormone based on studies of forearm metabolism in man. *Medicine* 42: 385-402, 1963.
10. Abrams, R. L., Parker, M. L., Blanco, S., Reichlin, S., and Daughaday, W. H., Hypothalamic regulation of growth hormone secretion. *Endocrinology* 78: 605-613, 1966.
11. Knobil, E., Pituitary growth hormone: adventure in physiology. *Physiologist* 9: 25-44, 1966.
12. Landon, J., Greenwood, F. C., Stamp, T. C. B. and Wynn, V., Plasma sugar, free fatty acid, cortisol and growth hormone response to insulin and comparison of this procedure with other tests of pituitary and adrenal function. II. In patients with hypothalamic or pituitary dysfunction or anorexia nervosa. *J. Clin. Invest.* 45: 437-449, 1966.
13. Blanco, S., Schlach, D. S. and Reichlin, S., Control of GH secretion by glucoreceptors in hypothalamic-pituitary unit. *Fed. Proc.* 25: 191, 1966.
14. Smith, G. et al: Effect of crude ovine stalk median eminence extract on plasma growth hormone in rhesus monkeys. Program of 48th meeting of Endocrine Society, June, 1966, p. 35.
15. Leeman, S. E. and Hammerschlag, R., Stimulation of Salivary Secretion by a factor extracted from hypothalamic tissue. *Endocrinology* 81:803, 1967.
16. McCann, S. M., Gonadotropic functions of the adeno-hypophysis. In *Physiological Controls and Regulations*. Edited by W. S. Yamamoto and J. R. Brobeck, pp. Philadelphia: Saunders, 1965, pp. 135-157.
17. Guillemin, R., Hypothalamic factors releasing pituitary hormone. *Rec. Progr. Hormone Res.* 20: 89-121, 1964.
18. Rothballe, A. B.: Some endocrine manifestations of central nervous system disease. *Bull. New York Acad. Med.* 42: 257-283, 1966.
19. Schally, A. V., Arimura, A., Bowers, C. Y., Kastin, A. J., Sawano, S. and Redding, T. W., Hypothalamic neurohormones regulating anterior pituitary function. *Rec. Progr. Hormone Res.* 24: 497-581, 1968.
20. Meites, J., ed., NIH Conference on the Bioassay and Chemistry of the Hypophysiotropic Hormones of the Hypothalamus: A Critical Evaluation, January 8-11, 1969, Williams and Wilkins, to be published.

Cancer

Could I have done more?
 I ponder—disturbed—uncertain.
 I did what I know—I am not God—
 A doctor trained—but not enough
 To stem the ravaged thrust
 Which thwarted us both—
 The victim—and me, his impotent shield.
 Could I have done more?

Fred F. Smith, M.D.

New Approaches for Study and Therapy of Cerebral Vascular Accidents

Guy Owens, M.D.

Can the site of cerebral vascular damage be accurately located? What therapy is indicated for cerebral vascular occlusion? How effective is the therapy when employed? Will the same therapeutic regime be effective in each patient? Since some stroke patients improve without therapy, how is it possible to claim benefits from treatment? The absence of answers to the above questions have contributed to the confusion over the care of acute vascular accidents. Recent technical developments seem to offer some help.

The Autofluoroscope

It would be helpful if cerebral vascular insufficiency or occlusion could be localized by diagnostic techniques. Contrast X-ray studies cannot identify small vessel occlusion, and so are inadequate in most stroke problems. Electroencephalography is of little value since it can identify damage only in a very gross fashion. Radioisotope techniques have offered some hope but with the older scanning devices the information obtained was static and usually identified only an area of blood brain barrier breakdown. The recent development of scintillation or gamma cameras has permitted a giant diagnostic stride to be taken. The Bender-Baird autofluoroscope¹ was one of these new devices used by Owens et al² for study of the brain circulation after intra-arterial injection of a radioisotope. This device visualizes an entire area or organ of radioisotope distribution at one time. Data can be collected every sixty milliseconds if desired. Greater amounts of very short-lived radioisotopes can be used which improve picture quality while maintaining a low radiation dose. Because of short exposure time and because the autofluoroscope is continuously sensitive to all areas within the field of view, rapid sequences of still pictures or time lapse motion pictures can be taken of subjects in which the distribution of radioactivity is changing.

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The autofluoroscope contains a mosaic of 294 sodium iodide crystals $1\frac{1}{2}$ inches thick, $\frac{3}{8}$ inches square, and arranged in a 14 x 21 rectangular array, 6 x 9 inches in size. Pulses occurring simultaneously in one of the 14 horizontal positioning photo tubes and in one of the 21 vertical positioning tubes uniquely identify the crystals in which the interaction occurred. A computer unit permits storage of up to 1000 counts per crystal location which can then be transferred to magnetic tape or for display to an oscilloscope. Data obtained from each crystal can be extracted every 60 milliseconds for transmittal to a strip chart. It is possible to identify from the oscilloscope areas about which quantitative information are desired. The details for such data retrieval have been reported elsewhere.¹ A region of the brain can now be selected and the isotope events which occurred within the vascular bed of that region can be observed over a selected time period. Without repeating the injection, similar observations can be made in adjacent areas merely by re-running the tape.³ Isotope count rates (dynamic quantitative flow studies) can then be compared and regions of slower or absent circulation identified. Data is preserved on tape for further study at any time. It is now possible to evaluate the cerebral arterial, capillary and venous phases of circulation in one or both hemispheres especially when intra-arterial administrations of an isotope is used. Circulatory variations can be more accurately identified giving us a new diagnostic dimension.

This tool can also serve as a means of determining therapeutic success but would prove cumbersome and expensive. Recent development of a second device has been reported by Woldring and Owens⁴ which appears to offer important monitoring advantages.

The Membrane-Mass Spectrometer

In vivo knowledge of gas exchange would be highly desirable for the physiologist and clinician. At the present time blood or tissue gases are measured by chemical analyses as originally designed by Bohr, Kragh, and Van Slyke. These measurements are indirect and require samples of blood or tissue

which are subjected to chemical extraction and absorption. The results are usually limited to concentration or saturation of oxygen and carbon dioxide only. More recently, physical and physical chemical techniques have permitted some improvement. These consisted of spectrophotometry of hemoglobin, oximetry, polarography and pH measurements of buffered solutions into which carbon dioxide was diffused. None of the above procedures permitted continuous recording of gas pressures *in vivo*. Each of these techniques was specifically designed for one gas only, excluding the possibility of simultaneous recording of different gases from the same location; most of them require samples of blood, which in effect, reduce their value to the equivalent of chemical analysis. These techniques cannot afford easy access to organs or remote locations of the body, which would be possible if a small measuring probe were to be used. None of the above techniques give any information in regards to parenchymal gas levels.

Measurement of nitrous oxide uptake by the brain, jugular blood pO_2 and saturation, thermal conductivity, and radioisotope studies have given data which has helped in the study of cerebral circulation. To date, none has permitted localized observation of cerebral gas exchanges and only indirect information on cerebral blood flow. Recent studies by Woldring, Woolford, and Owens,⁴ using a basically new technique for measurement of gas pressures in circulating blood opened new avenues for the study of gas exchange processes in blood and in tissue. With this technique, a cannula, closed at one end with a gas permeable membrane, was inserted into a blood vessel and connected to the inlet of a mass spectrometer. The pressure gradient across the membrane caused the blood gases to be drawn into the vacuum of a mass spectrometer; the rate of flow being dependent upon the permeability of the membrane and upon the partial pressure of each gas present. The mass spectrometer analyzed the gases simultaneously and instantaneously with a high degree of accuracy.

Because of the small probe size the vasculature of every part of the body can be made accessible. Any gas in the mass range of the spectrometer can be analyzed instantaneously, continuously, and if the mass spectrometer is so designed, simultaneously, with other gases from the same area. Using multiple probes and an appropriate switching arrangement it is even possible to sample from several sites at successive short intervals, in gas as well as in fluid or tissue (for example, venous, arterial blood, brain,

and alveolar air). In the study first reported, a rubber membrane was used. Initial efforts in measuring directly intracerebral gases were unsuccessful. When a cannula tipped by a rubber membrane was inserted in the brain tissue pO_2 levels dropped rapidly to zero while pCO_2 remained stable. It became apparent that the membrane vacuum system was competing with cerebral tissue for oxygen. Rubber, because of its diffusion properties, permitted rapid extraction of available O_2 which was not as rapidly replaced. This problem does not arise when measuring gas pressures in circulating blood partly because of the higher gas content of blood, but mainly because in this case gas diffusion does not present a problem since the tip is always in contact with fresh blood. Many different materials were tested. Teflon proved to be the best for intracerebral studies though analysis was considerably slower since gas diffusion was slow.⁵ Uses for this new device appear to be abundant: (1) Clinical diagnosis in respiratory or metabolic diseases where disturbances of gas exchange and of acid-base balance are found, (2) Monitoring of pO_2 and pCO_2 , as well as anesthetic level in blood during general anesthesia, (3) Gas dilution studies to measure blood flow, cardiac or tissue perfusion, (4) Gas pressures in lung, body fluids and blood during modified atmospheric conditions, (5) Tumor gas responses during radiation therapy and chemotherapy, (6) Experimental and clinical studies of oxygen pressures in areas of infarction and the alterations produced by specific therapeutic regimes. It would thus appear that this device now should be able to give answers to the questions posed at the beginning of this paper.

After studies have been finished using the auto-fluoroscope, the patient would then be taken to surgery where under sterile conditions and local anesthesia a cannula (No. 18 spinal needle) capped by a teflon membrane would be inserted through a burr hole into the previously identified vascular insufficient region by stereotactic technique. The cannula would then be fixed to the skull by a locking device and the patient returned to a special study center. Special tipped rubber cannulas could be placed percutaneously into a femoral artery and if necessary in the external jugular vein. The cerebral cannula and those in blood vessels would then be connected via copper tubing to a special mass spectrometer designed to give dual read-outs. Molecules entering the analyzing section of the spectrometer would be ionized, accelerated in a variable electric field, deflected in a constant magnetic field,

and projected to a target point (collector), upon which they would then confer their charges. Different molecular masses would be brought into focus by manipulation of the electrical parameters of the analyzer. The information would then be transferred to a multi-channel recording unit. Simultaneous systemic blood pressure records would also be obtained. When indicated electroencephalographic records would also be obtained. It has been shown experimentally, and it will be anticipated in clinical situations that such data would be collected continuously over many hours during specific therapeutic maneuvers. PO_2 , and pCO_2 and any special gas diffusion studies could be recorded. Therapy could then be instituted.

We have recently demonstrated that in dogs a 95% oxygen, 5% carbon dioxide gas mixture inhaled, significantly increases the pO_2 levels in the normal brain. It is superior to oxygen alone. It was shown in this study that the 95%–5% mixture protects the electroencephalographic activities for prolonged periods during serious arterial insufficiency.⁵ This information is not new. There, however, have been recent reports which indicate that additional CO_2 will not afford advantages in areas of infarction since maximum vasodilation has already taken place. Such information could be further identified in this type of study. Depending on

the pO_2 response during the use of a carbon dioxide–oxygen mixture other avenues of therapy might then be employed.

This monitoring technique would permit identification of therapeutic regimes which could rapidly be found to be successful in individualized instances. If no success was encountered, another therapeutic measure could be employed; and if nothing of any benefit occurred, therapy could be stopped at one's discretion. It appears, therefore, that a clearer indication of therapeutic effectiveness should now be available.

Bibliography

1. Bender, M. A. The Digital Autofluoroscope. In: *Recent Advances in Nuclear Medicine*, M. V. Croll and L. W. Bracy, Eds. New York: Appleton-Century-Crofts, 1966.
2. Owens, G., Bender, M. A. and Blau, M. Radioisotope (Gamma) Cerebral Angiography. *J. Neurosurg.* 28:466-470, 1967.
3. Fisk, J. R., Bender, M. A. and Owens, G. Experimental Cerebral Vascular Occlusion: A New Technique for Production and Method of Evaluation. In Press. New York St. J. of Med.
4. Woldring, S., Woolford, D. and Owens, G. Blood Gases: Continuous In Vivo Recording of Partial Pressures by Mass Spectrography. *Science* 153:885-887, 1966.
5. Owens, G., Woldring, S. and Belmusto, L. Continuous Intracerebral pO_2 and pCO_2 Monitoring by Mass Spectrometry. *J. Neurosurg.* In Press.

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LOUIS H. NAHUM, M.D., *Editor*

CONNECTICUT MEDICINE

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Blood Component Therapy

Edward E. Morse, M.D.

Introduction

The State of Connecticut, with its excellent Red Cross blood program, is in a significant position to make rapid progress in the provision of specific blood components for the treatment of patients with cancer, leukemia, anemia, infection and bleeding disorders. Over 100,000 units of blood are collected each year¹ by the Red Cross mobile units and distributed to hospitals within the State. It is a tribute to the Red Cross and the hospitals utilizing the blood that little of it is discarded. However, over 90 percent of the blood utilized is transfused as whole blood.¹ Such practice, while commonplace, is in itself wasteful. It has recently been stated in this journal,² "Almost all patients who need transfusion can be effectively treated with packed or sedimented red cells rather than whole blood."

In the last decade research in the blood fractions^{3, 4} and in supportive therapy for cancer chemotherapy,^{5, 6} as well as special programs developed by the Navy to provide frozen blood products,^{7, 8} have demonstrated the feasibility of separating whole blood into its various components. The specific component of blood required for the treatment of a given patient can be administered in higher concentration, in less volume, often with greater safety, and thus more effectively, than can be accomplished with the transfusion of whole blood. The increasing availability of blood components and fractions presents a challenge to those responsible for the education of medical students and house officers as well as to those responsible for the primary care of patients in Connecticut's hospitals to be exact in their diagnosis and more specific in their treatment of patients with blood diseases. The application of methods and knowledge developed through research in the area of blood components depends upon the awareness and enthusiasm of the physicians caring for patients requiring such therapy. If a diagnosis is clearly established and a need for a specific therapy delineated by appropriate laboratory tests, the blood collected can be put to broader use.

Concentrated Red Blood Cells

The prime example of component therapy is the use of concentrated red cells in the treatment of anemia due to causes other than active hemorrhage. Concentrated red cells are harvested by allowing the cells to sediment at 4°C for several hours or overnight in the blood bank refrigerator. When the plasma is removed, enough remains so that the hematocrit is seldom more than 70 percent.⁹ It is unfortunate that the term "packed cells" has been applied to all forms of blood from which some plasma has been removed. Most "packed cells" are merely concentrated. These concentrated red cells are as well preserved in the small volume of plasma as cells in whole blood,¹⁰ but they have the advantage that a greater increase in the recipient's hematocrit can be expected than with the administration of the same volume of whole blood. It has been pointed out that such therapy is advantageous in the elderly and in severely anemic patients.¹¹ More recently it has been recognized that concentrated red cells are useful in many other situations¹² and should be used for therapy whenever volume replacement is not an important requirement. Such units are suitable for cell replacement even in the patient undergoing surgery where blood loss is moderate. Table I illustrates four examples of patients treated during surgery with concentrated red cells (CRBC) and Hartman's solution. Blood lost was replaced volume for volume with CRBC. The hematocrits of the patients tended to be maintained in the high normal range by the design of the study, but no decrease in platelet count, coagulation factors or proteins was found when only the red cells were replaced. Truly "packed cells" can be obtained by centrifugation and removal of 80 to 90 percent of the plasma. Packed cells are useful for the treatment of patients who have allergic reactions to plasma products. For transfusion of severe reactors the cells are often washed 2 or 3 times with isotonic saline to remove traces of plasma, platelets and leukocytes. Packed cells are sometimes used when blood of the same ABO group is not available and it is desirable to reduce the amount of antibody¹⁰ in transfused blood. Packed cells of group O blood will function in the emergency as "universal donor" cells if the plasma antibodies have been substantial-

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TABLE I

Patient	CRBC ml	Hartmans Solution ml	Hematocrit %			Platelets 10 ³ /cmm			Fibrinogen mgm/100 ml			Albumin gm/100 ml		
			1	II	III	1	II	III	1	II	III	1	II	III
			IS Thoracotomy	300	1900	48	50	48	145	143	157	157	270	450
JC Bladder Resection	900	1900	43	49	48	278	233	212	500	440	500	4.0	4.3	4.0
WV Radical Neck	1200	2000	39	46	47	268	340	263	250	220	270	4.3	4.2	3.9
TS Aortoiliac Bypass	1200	2700	28	41	37	175	134	141	350	210	310	3.8	4.8	3.8

Legend: Estimated blood lost was replaced with concentrated red blood cells. Hartman's solution (Ringers with Lactate) was infused at the discretion of the anesthesiologist. The elements listed were measured: I—just before surgery; II—at the completion of the operation; and III—the next morning.

ly reduced by removal of the plasma. Since the administration of packed cells is slow, saline or another physiologic solution is added in small amounts to improve flow. Packed cells are currently being used in some centers for longterm freeze-storage.¹³

The use of whole blood should be reserved for those situations in which rapid volume replacement as well as red cell replacement is required and in situations where there is a reduction in multiple blood factors. The four major areas where such replacement is necessary are shown in Table II. Even in these clinical circumstances, the physician's judgment is paramount in determining the need for transfusion. For example: when hemorrhage is severe and continuing, freshly drawn whole blood may be required. On the other hand, if bleeding is not severe, careful follow-up may be all that is required, even when multiple coagulation factors are depressed as in hepatic insufficiency or in the defibrination syndrome. Certain clotting components such as platelets, fibrinogen and antihemophilic factor cannot be effectively replaced by administration of fresh whole blood alone. It is good practice to determine what specific defects exist so that supplementary therapy with the required fraction can then be given.

Platelets

Of the cellular elements of the blood other than red cells, the platelets are the most readily sepa-

rated.⁵ The entire volume of platelets from a pint of blood can be concentrated to a volume less than 20 ml. The platelets from 6 pints of fresh blood can be administered in a volume of about 100 ml and supply the needs of a thrombocytopenic adult for several days.¹⁴ New centrifuges are available to provide platelets in large amounts from single donors to obviate the risks of multiple donor exposure.¹⁵ The etiology of the thrombocytopenia in a patient is a major consideration in determining whether platelet transfusions should be instituted.¹⁶ Patients who have thrombocytopenia due to an immunologic abnormality as in Idiopathic Thrombocytopenic Purpura or Lupus Erythematosus usually do not benefit from platelet transfusions because the survival time of the platelets is markedly shortened.^{16, 17} However, even these patients may be transiently benefited by such therapy during splenectomy or in the event of cerebral hemorrhage. Platelet transfusions are usually reserved for patients who manifest bleeding in association with marrow failure as in aplastic anemia, leukemia or during cytotoxic therapy. The risk of life-threatening hemorrhage increases as the platelet count decreases.¹⁸ Platelet counts below 1000 are particularly dangerous since intracerebral hemorrhage may occur.¹⁹ The usual indication for platelet transfusion is major hemorrhage due to thrombocytopenia. When the platelet count is rapidly decreasing and falls below 10,000/cumm or when it reaches a level as low as 1000/cumm, it is wise to anticipate a hemorrhagic catastrophe and use fresh blood or preferably platelet concentrates as a precautionary measure. The effectiveness of the platelet transfusion depends primarily on the number of platelets given.²⁰ In the treatment of adult patients with acute leukemia, platelets from 5 to 10 units of blood are given every 2 to 3 days to maintain a platelet count over 20,000/cumm during the acute phase of chemotherapy.²¹ The same situation might

TABLE II

CLINICAL CIRCUMSTANCES REQUIRING WHOLE BLOOD

1. Massive Gastrointestinal Hemorrhage
2. Surgical Shock
3. Exchange Transfusions (as in open heart surgery)
4. Multiple Coagulation Defects associated with hemorrhage (as in hepatic insufficiency or defibrination syndrome)

be expected to hold for patients with acute marrow aplasia due to drug reactions. Since the platelets do not survive under the usual blood bank storage conditions for much over 24 hours²² they must be separated from the blood in the fresh state and utilized immediately or stored frozen in dimethylsulfoxide or in low concentration of glycerol.²³

Leukocytes

Transfusion therapy with leukocytes, in contrast to red cells and platelets, has not progressed rapidly because of the large number of cells required^{6, 24} and the relative paucity of these cells in the peripheral blood. Granulocyte transfusions have been limited to experimental approaches utilizing cells from patients with chronic myelocytic leukemia.^{6, 24} Only a few centers have undertaken the arduous task of collecting and transferring normal granulocytes.²⁵ A dose of about 1×10^{11} is required to produce defervescence and clearing of the blood of bacteria in patients with septicemia.²⁶ Individual patient response to leukocyte transfusion in terms of the number of cells that circulate following transfusion is highly variable. Many factors which have not been well studied influence the outcome of the leukocyte transfusion. Among those factors observed to affect the post-transfusion circulation of transfused leukocytes are the dose given, and the circulating granulocyte level at the time of transfusion.⁶ In one study, the ABO group of the leukocyte donor and the recipient did not appear to be important factors as long as the plasma and red cells were removed from the leukocyte preparation.⁶ Clearing of septicemia appeared to require a circulating granulocyte level above 1500/cumm.²⁶ It is clear that granulocyte transfusion therapy can be beneficial in patients with septicemia and leukemia. On the other hand, the possibility of transplantation of donor cells and graft versus host reaction still exists. Schwarzenberg observed symptoms and signs attributable to graft versus host reaction in several of the patients he treated with granulocyte transfusion.²⁴ Survival of transfused cells in the marrow as demonstrated by change in ABO blood groups has been reported.²⁷ More definitive separation of stem cells, lymphocytes and granulocytes will be required before these problems can be solved. Continuous flow centrifuges are currently being utilized in attempts to accomplish this feat.²⁸ The mechanical aspects of blood cell separation are gradually being solved. Leukocyte transfusions cannot be given with the same degree of safety and reliability as red cell transfusions. Leukocyte typing is in its infancy and antisera are not generally avail-

able. Procedures for a compatibility crossmatch for leukocytes require tissue culture procedures and staining with supravital dyes to determine cytotoxicity or cell death. "Natural" leukocyte antibodies do not appear to be prevalent, but before undertaking leukocyte transfusions it is important to know not only whether the patient's immune system will reject the donor leukocytes, but even more imperative, whether the donor lymphocytes will reject the patient's tissues. Although some evidence exists that leukocytes do not contain all the important transplantation antigens²⁹ their ready accessibility makes it likely they will remain the primary cell for antigen testing. It is likely that leukocyte transfusion and indeed tissue transplantation will be successful between the donor and the patient, if no evidence of interaction is found after donor lymphocytes are incubated in tissue culture medium with recipient lymphocytes.³⁰ Once antisera are generally available to detect the major histocompatibility antigens, the preliminary screening of donor and patient leukocytes with antibodies will make the tissue culture "crossmatch" feasible for many hospitals.

With the presently available techniques, lymphocytes are more readily separable from whole blood than are granulocytes.²⁸ The size and specific gravity of the lymphocyte is probably responsible for the different sedimentation characteristics of these cells.³¹ Experimental immunotherapy against tumor^{32, 33} is currently under study utilizing lymphocyte transfusions.

Plasma Fractions

Plasma fractions which have been available for some time include albumin, fibrinogen and gamma globulin. Albumin is a preparation which has been heat treated (60°C 10 hours) and is free of hepatitis virus. It is widely used for volume expansion and protein replacement. Fibrinogen is a concentrated (2 grams/100 ml) preparation which is used only in severe bleeding episodes following complications of pregnancy, various carcinomas, sepsis or the defibrination syndrome. Although it is an effective product, the risk of serious hepatitis is 11-25%³⁸⁻⁴⁴ Gamma globulin is a concentrated (16 grams/100 ml) preparation of immunoglobulins of mixed specificity which is effective in modifying or preventing a number of infectious diseases. It must be administered intramuscularly but, like albumin, it is free from risk of hepatitis. Cryoprecipitate, rich in antihemophilic factor (AHF), is precipitated from plasma by quick freeze and slow thaw of plasma.² The remaining plasma can be further

fractionated. Glycine precipitated AHF³ is even more concentrated and has the added advantage of being free of blood group antibodies. Both types of preparation are effective in the treatment of hemophilia.^{35, 36} It has been suggested from preliminary studies that concentrated fractions of AHF be used in the prevention of crippling bleeding episodes in hemophilia,³⁷ a hope patients with hemophilia have had for years. The obvious advantages of daily injections of concentrated AHF to maintain normal hemostasis in the hemophiliac are vitiated to some degree by the expense of the material and the lack of large amounts of the product. The tremendous quantities of plasma necessary for such a prophylactic therapy program could not be supplied unless much of the blood now being collected was fractionated soon after it was taken from the donor. It is estimated that there are about 12,000* hemophiliacs in the United States one tenth** of whom have bleeding severe enough to be considered for prophylactic therapy. If two units a day will prevent bleeding³⁷ altogether, about 900,000 units a year would have to be available. Substantially less might be required if treatment were instituted only at signs or symptoms suggesting early bleeding.

The hepatitis rate associated with glycine precipitated AHF has not yet been established. It is possible that the population of hemophiliacs being treated may be exposed to enough transfusion early in life to produce subclinical hepatitis and life long immunity. Furthermore, the process of glycine precipitation may alter the risk of virus transmission in factor VIII preparations from that observed with fibrinogen preparations. These speculations remain to be explored.

The prevention of hepatitis associated with administration of blood products by the use of gamma globulin is still a controversial issue. Two aspects of the problem are of vital interest. The first is the question of whether transfusion hepatitis can be mitigated or prevented by gamma globulin administration.^{38, 39} The second is lack of availability of the vast quantities of gamma globulin that would be required. The latter point has been used as an excuse for not considering prophylaxis for transfused patients. Regarding the first aspect, Mirick's study³⁸ indicated that two doses of gamma globulin, 10 ml each, one given within a week of transfusion and one a month later would prevent icteric he-

patitis but not the subclinical chemical abnormalities. The study of Holland and Schmid³⁹ showed that in patients receiving large amounts of blood for open heart surgery, icteric hepatitis was not prevented by two 10 ml doses of gamma globulin, but they gave the first dose just prior to transfusion. They suggested that the time of administration of gamma globulin may be important to the protective effect of passively administered antibody. Other studies^{40, 41} have shown at least a modifying effect on post-transfusion hepatitis when 20 to 30 ml of gamma globulin is administered in divided doses—*after* the exposure to transfusion. The evidence presented by Allen and Sayman⁴² that patients over the age of 40 receiving multiple transfusions are at greater risk of fatal hepatitis than younger patients merits further consideration in selecting recipients who might be given prophylactic gamma globulin. Patients who receive fibrinogen should definitely be given gamma globulin and "high risk" patients should be considered for prophylaxis. "High risk" is defined as those patients over 40 receiving more than one transfusion who have debilitating diseases, particularly those involving the liver. The task of providing all the gamma globulin for such prophylaxis can be approached along lines similar to those for the provision of platelets and antihemophilic factor. If sixty percent of the blood currently being collected were fractionated as a routine, enough gamma globulin would be produced to treat all the "high risk" transfusion recipients. The question of prophylaxis for post-transfusion hepatitis in the state of Connecticut is largely an academic one at present since the hepatitis rate is estimated to be less than 0.06 percent.⁴³ Other states³⁹ and other countries,⁴⁴ however, are not so fortunate. Hepatitis has occurred at rates between 11% for icteric and 60% subicteric in these studies.

Newer Components

Gamma globulin is now being produced from the plasma of recently immunized individuals for the treatment of generalized vaccinia⁴⁵ (Vaccinia Immune globulin) and for the prevention of Rh immunization in Rh negative mothers of Rh positive babies⁴⁶ (anti Rh immunoglobulin). These advances indicate specific antibodies can be produced readily and suggest another approach to the specific treatment of disease with a specific blood component.

Another coagulation product, Prothrombin complex, is also in clinical trial⁴⁷ and promises to be effective in the therapy of liver diseases, Vitamin K

* Factor VIII deficient patients estimated from Hemophilia Foundation registration.

** Patients with severe Factor VIII deficiency who have been hospitalized estimated from reported cases.

deficiency, overdose of dicoumeral drugs and hemophilia B (Factor IX or PTC deficiency). This plasma fraction is a by-product of the cold ethanol extraction of other plasma products and contains a concentrate of the stable Vitamin K dependent factors, Prothrombin (II), Stable factor (VII), Christmas factor (IX), and Hageman factor (X). It should be particularly effective in treatment of bleeding in severe chronic liver disease and in Christmas disease.⁴⁸

Summary

Blood transfusion as a treatment in medicine is gradually giving way to specific component therapy requiring careful diagnosis of the specific cell or plasma defect.

The availability of many of the labile products (platelets, leukocytes, and antihemophilic factor) requires their immediate separation from whole blood prior to storage. To make available other plasma fractions such as albumin, gamma globulin, and stable clotting factors, a much more extensive utilization of concentrated red blood cells is required so that the plasma can be harvested and fractionated. Concentrated red cells can, like other specific components, provide the needed product in greater concentration and in less volume, with greater versatility and effectiveness than whole blood.

Bibliography

1. American National Red Cross Blood Program Report, 1967.
2. Bove, J. R., Packed Red Cells, editorial, *Conn. Med.* 32: 428-9, 1968.
3. Pool, J. G., and Shannon, A. E., Production of high potency concentrates of antihemophilic globulin in a closed-bag system. *NEJM*, 273:1443, 1965.
4. Wagner, R. H., McLester, W. D., Smith, M., and Brinkhous, K. M., Purification of antihemophilic factor (factor VIII) by amino acid precipitation. *Thromb. Diath. Haem.*, 11:64, 1961.
5. Freireich, E. J., Kliman, A., Gaydos, L. A., Mantel, N., and Frei, E., Response to repeated platelet transfusion from the same donor. *Ann. Int. Med.*, 59:277-287, 1964.
6. Morse, E. E., Freireich, E. J., Carbone, P. P., Bronson, W., and Frei III, E., The transfusion of leukocytes from donors with CML to patients with leukopenia. *Transfusion*, 6:183-192, 1966.
7. Valeri, C. R., Bond, J. C., and McCallum, L. E., Relationships between metabolic state and (1) In vivo survival and (2) density distribution of previously frozen human erythrocytes. *Transfusion*, 6:543-553, 1966.
8. Moss, G. S., Valeri, C. R., and Brodine, C. E., Experience with frozen blood in combat casualties. *NEJM*, 278:747-52, 1968.
9. Mollison, P. L., *Blood Transfusion in Clinical Medicine*, 4th ed., F. A. Davis, Co., Philadelphia, Pennsylvania, 1967, pp. 57.
10. Valeri, C. R., Clinical effectiveness of concentrated liquid stored red cells and previously frozen red cells. *Maryland State Medical Journal*, 17:59-64, 1968.
11. Mollison, P. L., *Blood Transfusion in Clinical Medicine*, 4th ed., F. A. Davis Co., Philadelphia, Pennsylvania, 1967, pp. 53.
12. Wintrobe, M. M., *Clinical Hematology*, 6th ed., Lea and Febiger, 1967, pp. 389.
13. Huggins, C. E., Frozen blood-therapy and practice, *JAMA*, 193:941, 1965.
14. Levin, R. H., Pert, J. H., and Freireich, E. J., Responses to transfusion of platelets pooled from multiple donors and effects of various techniques of concentrating platelets. *Transfusion*, 5:54-63, 1965.
15. Tullis, J. L., Eberle II, W. G., Bandanza, P., and Tinch, R., Platelets-pheresis: Description of a New Technique. *Transfusion*, 8:154-164, 1968.
16. Jackson, D. P., Indications for platelet transfusions. *Maryland State Medical Journal*, 17:78-79, 1968.
17. Sprague, C. C., Harrington, W. J., Lange, R. D., and Shapleigh, J. B., Platelet transfusions and the pathogenesis of idiopathic thrombocytopenic purpura. *JAMA*, 150:1193, 1952.
18. Gaydos, L. A., Freireich, E. J., and Mantel, N., Quantitative relationship between platelet count and hemorrhage in patients with acute leukemia. *NEJM*, 266:905-980, 1962.
19. Morse, E. E., Zinkham, W. H., and Jackson, D. P., Thrombocytopenic purpura following Rubella infection in children and adults. *Arch. Int. Med.*, 117:573-579, 1966.
20. Djerassi, I., Farber, W., Evans, A., Transfusions of fresh platelet concentrates to patients with secondary thrombocytopenia. *NEJM*, 268:221-226, 1963.
21. Serpick, A. A., and Miller, W. R., The use of platelet transfusion in the treatment of leukemia. *Maryland State Medical Journal*, 17:80-83, 1968.
22. Levin, R. H., and Freireich, E. J., Effects of storage up to 48 hours on response to transfusions of platelet-rich plasma. *Transfusion*, 4:251-256, 1964.
23. Pert, J. H., Lundberg, A. S., Yankee, R. A., Henderson, E., and Zucker, M. B., Laboratory and clinical results with improved methods of preparing fresh and frozen platelets. *Maryland State Medical Journal*, 17:84-85, 1968.
24. Schwarzenberg, L., et al. Study of factors determining the usefulness and complications of leukocyte transfusion. *Amer. J. Med.*, 43:206-13, 1967.
25. Zhavoronkova, L. A., et al, The use of transfusion of freshly preserved blood and leukocytes in patients with tumors of the female genitalia during radio-therapy. *Med. Radiol. (Moskva)*, 11:40-44, March, 1966.
26. Frei, E., Levin, R. H., Bodey, G. P., Morse, E. E., Freireich, E. J., The nature and control of infections in patients with acute leukemia. *Cancer Research*, 25:1511-1515, 1965.
27. Bronson, W. R., McGuinness, M. H., Morse, E. E., Hematopoietic graft detected by a change in ABO group blood. 23:239-249, 1964.
28. Freireich, E. J., et al, Separation and collection of leukocytes. *Cancer research*, 25:1516-20, 1965.
29. Brand, K. G., Chiu, S. Y., Silberman, G., et al, Antigenic analysis of human cells and tissues: Immuno-diffusion studies on liver tissue, white blood cells and subcellular fractions. *J. of Immunol.*, 99:1042, 1967.
30. Van Rood, J. J., and Eermisse, J. G., The detection of transplantation antigens in leukocytes. *Seminars in Hematology*, 5:187-214, 1968.
31. Noble, P. B., Cutts, J. H., and Carroll, K. K., Ficoll

flotation for the separation of blood leukocyte types. *Blood*, 31:66-73, 1968.

32. Schwarzenberg, L., et al, Attempted adoptive immunotherapy of acute leukemia by leukocyte transfusion. *Lancet*, 2:365-8, 1966.

33. Symes, M. O., Riddell, A. G., Immelman, E. J., and Terblanche, J., Immunologically competent cells in the treatment of malignant diseases. *The Lancet*, 1:1054-1056, 1968.

34. Mainwaring, R. L., and Brueckner, G. G., Fibrinogen transmitted hepatitis. *JAMA*, 195: 437-441, 1966.

35. Schwartz, J. M., Cohn, B. D., Ritz, N. D., Levy, T., Appendectomy in hemophilia with the use of cryoprecipitated human factor VIII to control bleeding. *JAMA*, 198:1175-1179, 1966.

36. Abildgaard, C. F., et al, Treatment of hemophilia with glycine precipitated factor VIII. *NEJM*, 275: 471-475, 1966.

37. Robinson, P. M., Tittle, P., and Smiley, R. K., Prophylactic therapy in classical hemophilia. *The Canadian Medical Association Journal*, 97:559-561, 1967.

38. Mirick, G. S., Ward, R., and McCallum, R. W., Modification of posttransfusion hepatitis by gamma globulin. *NEJM*, 273:59-65, 1965.

39. Holland, P. V., Robinson, R. M., Morrow, A. G., and Schmidt, P. J., Gamma globulin in the prophylaxis of post-transfusion hepatitis. *JAMA*, 196:471-474, 1966.

40. Grossman, E. B., Stewart, A. G., and Stokes Jr., J. S., Posttransfusion hepatitis in battle casualties and a study of its prophylaxis by means of human immune serum globulin. *JAMA*, 129:991-994, 1945.

41. Torli, A., Shoji, N., and Miyazato, Y., The use of gamma globulin for the prevention of serum hepatitis. 10th Congress of International Society of Blood Transfusion. Stockholm, Sweden.

42. Allen, G., and Sayman, W. A., Serum hepatitis from transfusions of blood. *JAMA*, 180:1079-1085, 1962.

43. Bove, J. R., Delayed complications of transfusions. *Conn. Med.*, 32:36-39, 1968.

44. Shimizu, Yoshitaka, and Kitamoto, Osamu, The incidence of viral hepatitis after blood transfusions. *Gastroenterology*, 44:740, 1963.

45. Report of the Committee on the Control of Infectious Diseases, 1966, pp 125. American Academy of Pediatrics.

46. Symposium: Immunologic suppression of primary Rh antibody formation, *Transfusion*, 8:125-153, 1968.

47. Tullis, J. L., and Pennel, R. B., Transfusion of specific plasma components. *Ann. Rev. Med.* 19:233-46, 1968.

48. Tullis, J. L., Melin, M., and Jurigian, P., Clinical use of human prothrombin complexes. *NEJM*, 273:667-74, 1965.

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Development of Patient Care in the School of Medicine

James E. C. Walker, M.D.

One of the foremost issues facing American medicine today is the application gap. Methods must be developed whereby the advances in health sciences can be applied more directly to the health care needs of society. This issue must be a principal concern of the university which looks to assuming leadership in the future. A medical school which is beginning, and therefore has the special advantage of being unfettered by tradition, has a special opportunity to examine this kind of issue and to make special contributions.

The original planning staff of The University of Connecticut School of Medicine, which consisted of an anatomist, an obstetrician, a psychiatrist, a physiologist, and later an internist, had a deep concern about the application gap. They began by exploring "the needs of the patient" and proceeded to design a model for care around these needs. The curriculum and the patterns of care in the Medical School were then developed. This planning process, beginning with the patient, has resulted in certain concepts which are unusual among schools of medicine. This report will review this planning process, beginning with the patient and extending to the model for care developed. It will then outline the specific departures taken by this School as a result of incorporating these concepts into the curriculum and organizational structure of the School.

Needs of the Patient

In general, the patient would like the best possible care accessible to him, available when needed, and provided in the most personal and comfortable manner. These needs might be categorized as the three A's: Ability, availability and acceptability. They would be given different priority by different patients and many patients might judge "ability" using different criteria from those used by most physicians. The planning staff's view of these needs was as follows:

Ability—Highly competent care in this era, and in the future, rests first on the utilization of all

current knowledge and techniques available for the best care of the patient's particular illness. Because this body of knowledge cannot be encompassed by a single mind, the utilization of specialists, who have knowledge in depth about specific organ systems and illnesses, is mandatory for excellent care. At the same time, competent care usually requires attention to more than a single organ system. When multiple systems are involved, and especially when emotional and/or social factors are involved, the need to coordinate the efforts directed toward solving these multiple problems, viewing the patient as a whole person, is essential. In addition, competent care in the future also will require an enlightened concern with improving the opportunities for health before illness appears, that is preventive medicine. These ingredients of competent care, specialized, total and preventive care, have been termed "comprehensive care." In the view of the planning group, comprehensive care and competent care become synonymous if medicine is to meet the mandate of "ability" in the future.

Availability—The patient desires care which is readily and financially available to him. This requires that care resources either be distributed geographically according to intensity of need, or be made accessible by transportation mechanism, and that there be no financial barrier to care. In addition to geographical and financial availability, care also must be accessible on a 24-hour basis. Because a single provider of care cannot constantly be available, the creation of a system whereby an alternate or substitute for the single provider must be considered. The establishment of groups consisting of physicians and related professionals has been a popular mechanism for meeting this need of availability in the past. In addition to the formation of groups, economy requires that certain tasks related to care be assigned to that member of the group most able to handle it with the least expensive education. Any advances in delivering care which could increase availability for the patient, without jeopardizing ability or acceptability, were considered legitimate.

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Acceptability—In addition to convenience, comfort and pleasant surrounding, the patient desires the most pleasant personal relationships in receiving health care as possible. For some patients this means a continuing relationship with an individual whom they trust, like and can communicate with. Indeed, continuity of care may foster competent care through augmenting the physician's understanding of the patient and his illness. On the other hand, changing patient-physician relationships may provide new points of view and information which may be desirable to improve care. The planning group agreed that continuity of care was generally important from the points of view of both the providers of care and the patient, and that it could be best preserved by identifying a personal physician for the patient or, at the least, minimizing the number of individuals responsible for advising him.

A Model for Care

After visualizing the needs of care from the patient's point of view, the planning staff attempted to define a model for rendering care that might best meet these needs. This process was done with a view to the current trends in medicine and society, but no attempt was made, at this point in planning, to have such a model conform to existing patterns in academic medicine.

Could the needs of patients, as defined, be met by the development of a better "system" of rendering medical care? Industry, for example, has developed systems which meet consumer demands that are not unlike the patient needs described above. Medicine, like industry, has developed its specialties as knowledge and technology have advanced but in this process has overlooked at least the following ingredients to make the system meet patient needs: a first contact point to permit the patient entry into the system; a mechanism for coordinating care among specialists and interpreting therapy to the patient; a resource for providing care not requiring the expertise of the present day specialist; a focus on those elements of care not provided by developing specialties, that is, the psychosocial aspects of care and a special focus on the family and maintaining the health of its members.

The analysis made clear that medicine in its advancement had not developed the system, or perhaps the "special role," that would replace many of the functions assumed in the past by the generalist. Trends made it equally clear that the ranks of the general practitioner were being rapidly depleted. The planning staff suggested four alternatives for

filling this role. *First*, could an associate degree physician, like the feldsher developed in Yugoslavia, fill the first contact role? It was agreed that most patients would accept a physician's assistant, but most would probably not accept a substitute for a physician. For example, the midwife has not been accepted in most parts of this country. Furthermore, the role as defined was a special and complicated one requiring at least as much education as received by present-day physicians. *Second*, could specialists working in a group fill this role by working together, and at the same time meet the needs of specialty care and consultation? This was felt to be a possible alternative but not ideal in that combining both roles in one individual could jeopardize the development of excellence in each. *Third*, could the defined needs of care be met by existing general practitioners or by primary or family physicians. Here the planning group was concerned about the breadth of the role required. Could one individual, in this era, provide with competence adult and child care, "normal" obstetrics and "applicable" surgery and still adequately meet the needs of comprehensive, continuing care? Rejecting this, the planning group settled on the *fourth* alternative which combined some of the elements of the other three. Accepting the current strong trend toward specialization, and seeing nothing on the immediate horizon to indicate the creation of a new category of physician who might meet the defined needs, the planning group looked to those specialties which might most easily incorporate the needed breadth of competence. Pediatrics and Internal Medicine are the broadest specialties of the present era and focus on the whole child or adult while avoiding areas such as Surgery and Obstetrics where special, highly technical skills are required. Medicine and Pediatrics, unlike other specialties, have primary care responsibilities which might be extended to meet the broad needs of care through the formation of teams which could include skilled members of the allied health professions. Such a group, directed by the general internist and pediatrician, and including the nurse, social worker and perhaps the physician's assistant, might be strategically located to meet patients' needs, relying on the specialists as consultants, and focusing on the patient, family, his comprehensive care and preventive medicine.

This group, consisting of the general internist and pediatrician working with the health-related professions and utilizing the specialist for consultation, it was felt, could meet the patient's needs of

ability, availability and acceptability and might fill the growing application gap in the health care system. The individuals in such a group would have to maintain a continuing responsibility for their patients in the hospital as well as the office and the community if the needs of continuing and comprehensive care were to be met.

Incorporation of the Model into the Medical School

The planning group proceeded from the definition of patient care needs and the consideration of a model which could meet these needs, to explore mechanisms whereby such concepts could gain expression and strength in a school of medicine. This planning was accomplished along three fronts: Departmental organization, patient care responsibilities and the undergraduate and graduate curricula.

Departmental Organization—The usual structure of the three departments, Medicine, Pediatrics, and Preventive Medicine, was examined in light of the model for care which had been designed, and, at the same time, with a recognition that the future required increasing strength in the medical specialties and their research programs. These three departments were realigned to form Departments of General Medicine, General Pediatrics and a Department which would include the specialties of both Medicine and Pediatrics. The two general departments were to consist of generalists in their respective fields having broad interests in the providing and teaching of patient care. The responsibility for Preventive Medicine was incorporated in both these Departments with the view that its impact in teaching, and its opportunities for the development of models in health care would have greatest potential in a setting of clinical responsibility. The Department of Medicine and Pediatric Specialties was to bring together individuals with particular interests in the clinical and research aspects of their specialties, relating the specialties of Medicine and Pediatrics at their points of common concern. The other academic departments of Surgery, Psychiatry, Obstetrics-Gynecology, Radiology, Anatomic Pathology and Laboratory Medicine were established in the manner usual to most schools of medicine.

This realignment of departments provides several opportunities for development. For the specialties of Medicine and Pediatrics, it not only provides greater opportunity for interrelationships at points of common interest, but allows the specialties to be pursued in greater depth both in the laboratory and the clinical setting. The general departments of Medicine and Pediatrics have the opportunity

of gathering strength in the practice and teaching of clinical medicine and the opportunity to develop and evaluate new programs in patient care and community health.

Patient Care—The incorporation of this model for care into a health center would assign the responsibility for direct, continuing care to the general pediatrician and internist, and the responsibility for consultation and special services to all other departments. Some modification of this model is necessary because the special needs of all clinical departments require some direct care responsibility to meet their needs of teaching and investigation. The general departments were therefore assigned the responsibility for care of patients *self-referred* to the clinics or emergency ward, and were to maintain a continuing responsibility for providing care for these patients in or out of the hospital. The generalist will retain his responsibility for care, with consultation where required, up to the level of his competence and will refer patients for care to consultants when this point was reached. The specialty department, and other departments, will assume the principal responsibility for *referred* patients, maintaining this responsibility for care both in the clinics and the hospital, and returning the patient to his personal physician when this phase of care was concluded. These departments will also, however, assume continuing responsibility for a limited number of self-referred patients to the extent necessary for rounding out their clinical needs. When this responsibility is assumed, the specialist will become the managing physician, providing total care with consultation from others when necessary. Similarly, the general departments, in addition to providing care for the self-referred patient, might, in certain instances, provide consultation for patients referred from other departments, or from the community, when certain diagnostic problems or multi-systemed diseases were involved.

This general framework of care permits both the incorporation of the ideal model for care and increases the strength for the clinical, teaching, and research responsibilities of a school of medicine. The formation of general departments of Medicine and Pediatrics provides opportunity for focusing on the practice and teaching of clinical medicine and for evolving and investigating models of care. These generalists, by functioning in a pediatrician-internist team working with the health-related professions, can assume care responsibility which extends from the clinic, to the hospital and the community, and includes acute care at the emergency

service level and chronic care at the nursing home level. This continuity of care responsibility, unusual where staffing patterns tend to fragment health care, provides the faculty of generalists an opportunity to represent to the student by example rather than lecture, the ideals of patient care.

As important as are the ideals of patient care, a school of medicine also has the responsibility for advancing knowledge in the health sciences and for providing a resource of referral for its community at large. The creation of a department which focuses on the research and clinical aspects of the specialties, and the presence of general departments which meet a service and teaching demand that has often overtaxed the specialist, provides increased potential for the medical school to meet these traditional, important responsibilities. The specialist, operating from his specialty clinic, is available for referral as well as for consultation during hospitalization. He can also, to the degree important to his teaching and research obligations, assume full care responsibility for patients in his area of specialty, and must, as the generalist, assure that this care is continuing and comprehensive.

Curriculum—In the *undergraduate* curriculum, this model of patient care assumes importance in two major areas. The *first* is The Introduction to Clinical Medicine, which extends throughout the first two years of the curriculum for one-half day each week, introducing the student to patients and their problems from his first month of school. This course includes elements of the behavioral sciences, psychiatry, community medicine and physical diagnosis, using the generalist in medicine and pediatrics as the primary preceptors for students. Students in groups of eight work with these two preceptors as they provide care for patients with the health-related professions in the framework of care described. The *second* curricular expression of this model is The Basic Clerkship which occupies six months of the third year. This course is designed as the required “core” of the clinical years and emphasizes the *process* of care common to any pursuit in medicine. Its concerns include the fundamentals of differential diagnosis, the usefulness and critical appraisal of diagnostic studies, the principals of therapy, and the understanding of the emotional components of illness, as well as an exposure to patients at all levels of care need. This Clerkship will focus on the role of the general pediatrician and internist who, because of the nature of their function, are natural preceptors for this experience.

The *graduate* curriculum will be flexible and will offer electives in subspecialties, and in research, not only in university hospitals, but in hospitals and clinics away from the University Hospital system. While emphasis will be on the model of responsible continuing patient care, residents and fellows will be given every opportunity to structure their graduate training in ways best calculated to help them attain their career goals in medicine. For example, combining medicine and pediatrics through elective rotations might lead to certification in both specialties, or toward broadening the base for careers as family physicians and primary physicians. Involving interns and residents from all departments in the common exploration of the basic sciences, research methodology, the sociology of health care, the behavioral sciences, and problems in health administration will emphasize the essential unity of the health professions and the need for team work in patient care.

Implications of Departures

The University of Connecticut School of Medicine has had a special opportunity to initiate certain departures from tradition. The advantages of its location, its relatively affluent setting, the sophistication of its community and the special advantage of beginning anew all provide it with an unusual opportunity for innovation. The departures it has been able to take as a result, are unusual among medical schools in this country and have certain implications that are worthy of examining.

It appears increasingly clear that schools of medicine will have to attract and provide academic rewards to physicians who are able and interested in practicing and teaching clinical medicine. This is necessary for at least the following reasons: If more practicing physicians are to be produced by schools of medicine, and the present “application gap” narrowed, students must be exposed to clinical teachers who represent attainable models of excellence. Second, because medical schools no longer hold captive the indigent patient, who before Medicare accepted the inconveniences of university clinics and emergency services for lack of another choice, they must now create facilities and attract individuals with the patient’s need in mind. The need for university hospitals now actively to compete for patients for their teaching services is a side effect of Medicare which should act to improve the services rendered. An important further effect of Medicare on academic medicine is that it provides an eco-

conomic resource, not available in the days of indigent care, to help support faculty involved in patient care. It is deserving of special emphasis that a medical faculty should be involved in the practice of medicine to the extent required to meet their responsibilities in teaching and research. The competition for patients between practicing community physicians and medical school faculty is not significant in that relatively few patients are involved. Further, faculty physicians at The University of Connecticut generate no personal income from practice.

The setting of Preventive Medicine in this School is also of some interest. Most departments of Preventive Medicine in this country have been separate from clinical departments. Attention in this School has been focused on presenting to the medical student the importance of personal preventive medicine, as well as environmental preventive medicine in the total scheme of community health care. For this reason it has been placed in the clinical setting of General Medicine and Pediatrics where its relevancy to direct patient care can become clear to students. Individuals interested in the behavioral sciences and research in the delivery of health care are working closely with clinicians and students and have the potential of relating their teaching and research closely to clinical problems.

Finally, the creation of separate departments which address themselves particularly to clinical teaching has important implications for the future.

This departure implies that medical schools in the past may not have been able to provide sufficient strength in patient care teaching through the model of the physician-scientist who has been presumed to have equally balanced research and clinical talents. If this is true, and if balance in teaching requires two groups of faculty members each emphasizing their particular skills, there exists a danger of these groups becoming separated. This separation could have the serious consequence of turning the clock backwards to the pre-Flexner era, and must be assiduously avoided. The general and specialty departments in Medicine and Pediatrics at this School will have many intertwined responsibilities in care and teaching and will play complementary roles in patient care. There will be constant interplay in the clinics and at conferences, house staff programs will be jointly administered, the pediatric and medical inpatient services will have patients of the general and specialty departments in the same physical setting, and attending rounds will be undertaken on all patients by members of both departments. These arrangements can foster the close relationships among these groups so important to sound development.

The outcome of many of the plans outlined in this report must await the tests of time and trial. If the potentials for success they have in this particular school are realized, their impact on the practice and teaching of medicine in this country may help set the pace for the future.

Intolerance for Discomfort

Americans before the Civil War looked on health much as the Greeks had. Illness, suffering and death were part of life. When illness struck, the physician and the patient entered into a partnership. Neither expected to overcome the threat alone. Each did what he could, and both hoped for nature's help. A century later this attitude had altered drastically. In effect, the patient abdicated his share of responsibility. The practicing man sees it daily—the executive who carries his nitroglycerine in a briefcase stuffed with homework, the victim of emphysema who begs for one last cigarette before his inhalation therapy, the fat lady who demands a pill that will permit her to enjoy both a winning figure and the eating habits of a Green Bay Packer. Neither physician nor patient is willing to put up with a few extra days of discomfort awaiting a certain cure by nature. The simple truth is that the American people no longer consider disease or even discomfort inevitable. In fact, it appears that many Americans are now psychologically quite prepared to accept the notion that death itself is no longer a necessary condition of life. (Robert P. Hudson, M.D., *Annals of Internal Medicine*, September 1967.)

The Educational Program of the University of Connecticut School of Medicine

Carl F. Hinz, Jr., M.D.

Taken in broadest context, the educational goal of the University of Connecticut Health Center is to prepare health personnel to meet the needs of our society. Since the Health Center initially consists of the Schools of Medicine and Dental Medicine, this mission is primarily directed to the education of physicians and dentists. However, it must be interpreted not only in the context of undergraduate professional education prior to the MD degree which is the usual responsibility of a university medical faculty. Clearly implied is an institutional commitment for major responsibility in all three periods of a physician's career: the undergraduate, house officer, and continuing education phases of medical education. The total faculty, designated at the University of Connecticut as the General Faculty, will develop policy regarding all three areas of education and these in turn will be implemented under appropriately designated associate deans.

At this early stage in the development at the Health Center the undergraduate programs are the ones most visible and therefore will be the primary subject of this discussion. Two major goals of the undergraduate program in medicine are apparent: First, to prepare the student properly for a career in a specified area of medicine. Second, to establish a proper climate or milieu for learning.

Educational Goals

Career Preparation

Both the enormous advances in science and the increasing breadth of services demanded by society have increased the number of career options open to individual medical graduates. Furthermore, there is an increasing tendency to make tentative career choices during medical school and to begin the branching or specialization processes prior to the MD degree. In light of these factors the institutional goal related to career includes the following components:

1. To develop in the student a sound understanding of the scientific basis of medicine. It is self-evident that competent health care must be based on a rational understanding of the pathophysiologic mechanisms of disease and therapeutic principles.
2. To develop in the student an appreciation of the nature of human behavior and an understanding of the elements of the doctor-patient relationship. Medicine is a social as well as a biologic science and involves intense interpersonal relationships both with patients and with colleagues. Therefore, understanding of the human personality is essential to proper practice.
3. To provide the student with a broad perspective on the health needs of the nation in their social, organizational, and economic contexts. There is a need to see beyond the organic aspects of disease and the makeup of the patient himself to appreciate that patient's relationship to society and the larger problems of the society itself.
4. To give the student adequate exposure to various career opportunities and to provide him proper guidance toward them. This requires both the availability of a variety of career models for the student and sufficient flexibility in program planning to permit the student to explore those avenues of interest to him. Considering this, it must be recognized that not all students will embark on exactly the same course of study during their undergraduate period.

The Climate for Learning

The second goal, the establishment of a milieu favoring learning, is also comprised of several parts:

1. The creation of a climate conducive to learning, wherein the faculty and students are colleagues pitted not against one another but with common direction toward mastery of a given area of knowledge, and where students cease to be competitors against one another.

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2. The development in the student of sound habits of self-education since these are so vital to continued learning during the many years of clinical practice following the termination of the formal period of education. This requires a shift in emphasis from teaching by the faculty to active learning by the students and demands development of programs of independent study.
3. The development of the student's skills in problem-solving. This, of course, has been repeated often, but re-emphasizes that the goal of a medical education is not the mere acquisition of facts but their rational application to the solution of clinical or other problems. Since all facts cannot be taught, a major emphasis must be placed on the processes by which knowledge is acquired and then applied to the solution of problems.

Operational Decisions Necessary for the Implementation of the Program

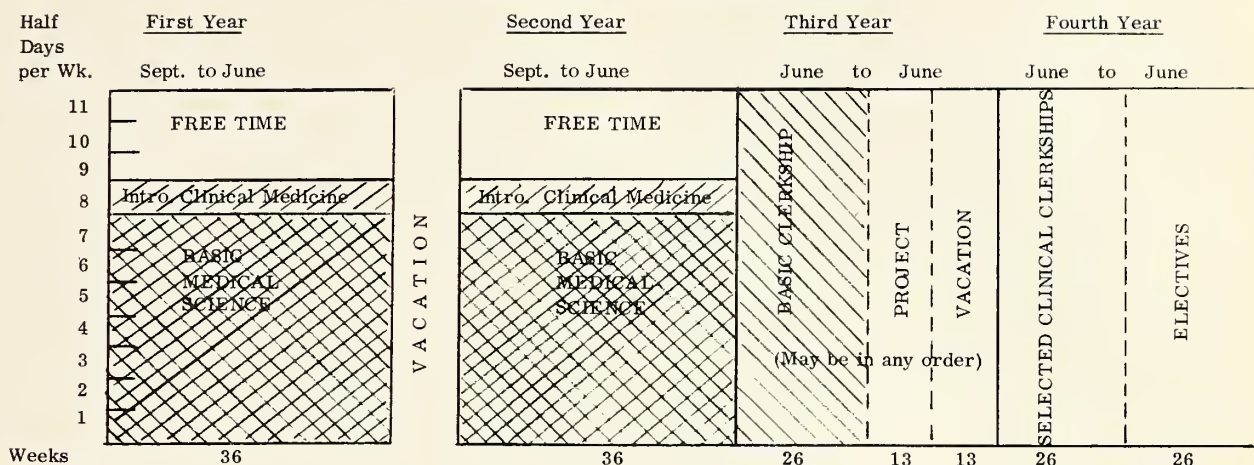
A number of operational decisions have been critical to the translation of the objectives into a coherent educational program. They are to some extent interlocking and each one has led inevitably to the next succeeding ones.

1. *General Faculty Responsibility for the Educational Program*
Instead of parceling out curricular time to autonomous individual departments, the entire faculty has assumed responsibility for the major decisions concerning curriculum. This has helped eliminate the traditional territorial prerogatives, and is seen as a means of developing a more integrated and cohesive program.
2. *Development of the Core Curriculum*
With the vast and ever increasing amount of medical knowledge, it is obviously essential that a great degree of selection be exercised to determine those activities which are to be included in a four year experience. The establishment of a core curriculum is required in both the basic sciences and the clinical areas. It is especially important if the tendency to schedule all available time is to be resisted so that students do have some opportunity for flexibility and selection in planning.
3. *Common Basic Medical Science Curriculum for Medical and Dental Students*
Based on the principle that dentistry has the same scientific basis as medicine, the dental

students participate in the basic medical sciences curriculum of the first two years. Thus the two groups are taught as a single class during that time. This has permitted the development of added strength in single basic science departments serving both schools.

4. *Organization of Teaching Around Functional Biologic Units*
Disease does not occur according to traditional academic discipline but rather according to disorders in various systems of the body. Teaching organized about organ systems gives the basic sciences greater relevance to clinical problems.
5. *Teaching by Interdisciplinary "Subject Committees"*
This arrangement brings faculty from a variety of clinical and basic science departments together to teach about biologic units including the molecular, cellular, tissue, organ, and whole body levels of organization. Such a plan allows integration among all disciplines and emphasizes the relevance of one discipline to another.
6. *Development of a Central Teaching Facility*
Accepting the premise of interdepartmental teaching, it is then logical to develop a centralized teaching unit to provide classroom, laboratory, and independent study areas so that the students have one central Multidiscipline Laboratory which represents their home base and to which the faculty members from various departments come to conduct their teaching. This arrangement has permitted increased efficiency in operation of teaching facilities, particularly the development of a skilled staff to operate the teaching facilities.
7. *The Introduction of New Departments*
This does not directly derive from the preceding points, but does stem from the stated institutional goals. It is necessary to provide professional models for the students so that they may make logical career choices. Since many students eventually fill the role of primary physician and since this role model has not been represented on full time medical school faculties, two departments have been created in the medical school. Both are staffed by individuals broadly skilled in their respective areas, but with a primary interest in the delivery of comprehensive patient care and

Figure 1
The Undergraduate Medical Education Program



in teaching about patient care. The Department of Clinical Medicine and Health Care consists of broadly based internists with additional members in sociology, epidemiology, and economics. Similarly, the Department of General Pediatrics is comprised of broadly based pediatricians with a primary interest in patient care. A third department, the Department of Medical and Pediatric Specialties, represents the more traditional medical school departments of medicine and pediatrics with individuals who have specialty interests and a strong investment in laboratory research.

The Medical Curriculum

The medical curriculum consists of four parts, the first two of which represent the core curriculum required of all students, the last two of which represent those programs in which students have a major degree of choice. (Figure 1) The Basic Medical Sciences of the core curriculum is two years in length; the basic clerkship, or core clinical experience, is six months in length. The optional portions of the curriculum are distributed throughout the entire four years and will be described below under the separate headings of selected clinical clerkships and free (or elective) time. It is important to emphasize that approximately 50% of the calendar time during medical school involves a significant degree of individual selection by the student. Furthermore the flexibility is such that the unusual student can complete all of his required activities in the course of three calendar years.

Basic Medical Sciences

The Basic Medical Sciences curriculum is organized on an interdisciplinary basis around func-

tional units, particularly the various organ systems. (Table 1) It is taught as a series of blocks by subject committees so that during any one period of time the students take only one course. Class time is scheduled for seven of the eleven half days each week, a total of 28 hours. The first course deals with general aspects of cellular and molecular biology approached from the point of view of normal structure, chemistry and function but with some emphasis on general pathologic processes. This is followed by study of tissue biology and general pathobiology, including greater emphasis on abnormal processes such as neoplasia, degeneration, inflammation, and the immune response. As seen in the tables, this initial study of general human biology occupies somewhat more than half of the

TABLE 1
SUBJECT COMMITTEES IN BASIC MEDICAL SCIENCES

	Duration (Weeks)
<i>General</i>	
Molecular and Cellular Biology	7
Tissue and Pathobiology	13
Biometry	1
<i>Organ Systems</i>	
Central Nervous System	7
Musculoskeletal System	4
Electives (First Year)	4
Renal-Urinary System	3*
Cardiovascular System	6*
Respiratory System	3*
Gastrointestinal System	6*
Hematopoietic System	3*
Endocrine-Reproductive System	7*
Integrating Mechanisms (Growth and Development)	4*
Electives (Second Year)	4*

* Approximate

first year, and ends with a brief course on biostatistics and biostatistical principles.

Thereafter, the teaching emphasizes the major organ systems beginning with the central nervous system and musculoskeletal system in the first year. The second year will be renal, cardiovascular, respiratory, gastrointestinal, hematopoietic, and finally endocrine-reproductive as a major integrating system. There will be a final integrating course developed around the theme of growth and development. In all organ system subject committees the teaching will be "back to back", that is the normal aspects of chemistry, physiology, anatomy, and pharmacology will be considered in relation to the abnormal or pathologic processes and their expression as clinical disease. The major emphasis will be on major pathophysiologic principles rather than on encyclopedic coverage of disease entities, but clinical descriptions and clinical correlations will be used extensively. This two year course then represents the didactic course in medicine, both from its fundamental and clinical point of view, for whole class teaching is not contemplated during the third and fourth years. The subject committees in the first two years provide approximately 2,000 hours of curricular time.

The Core Clinical Experience

Students will begin a limited clinical experience during the first two years in a course entitled Introduction to Clinical Medicine which occupies approximately one-half day each week. This course uses contact with the individual patient and his medical problems as the basis on which the student progresses toward the following objectives.

1. The development of a professional role with progressive assumption of responsibility for care of patients.
2. Development of perspectives on health care toward broader understanding of the social and cultural aspects of disease, the economic problems of health care, and the various means by which health care is delivered.
3. A better understanding of human behavior and the components of the doctor-patient relationship.
4. Development of skills such as physical diagnosis and history taking which are essential to good clinical care.

This experience leads to full time clinical activity for six months in the third year during the introductory or so-called "basic" clerkship. This will be based both on ambulatory and inpatient serv-

ices and will be conducted from the point of view of the primary physician providing comprehensive care. Thus, members of the Department of Clinical Medicine and Health Care and the Department of General Pediatrics will play a major role in the conduct of this clerkship which will focus on the case method and a preceptorial relationship with the faculty. There will be major contribution from the Department of Psychiatry and its emphasis on human behavior, and from the Departments of Surgery and Medical and Pediatric Specialties for their emphasis on pathophysiologic principles. Each student will be a member of a firm of physicians responsible for both inpatient and outpatient care so that he may have the opportunity to follow patients requiring hospitalization both before and after their admission. The "firm" concept should provide an emphasis on continuity of care as well as comprehensive care to reinforce the traditional emphasis on pathophysiology and correlation of basic science with clinical disease. During this six month period it is anticipated that the student will see a variety of patients and develop those skills which are broadly applicable to all the disciplines of medicine.

Selected Clinical Experiences

In addition to six months on the introductory clerkship, each student will be required to select six additional months of clinical clerkships according to his particular needs and career goals. Though most students will take clerkships in such major areas as surgery and obstetrics, there will be no prescribed set of clerkships for each student. Thus, some students may graduate without direct clinical experience in all major specialty areas. However, it must be emphasized that they will have exposure to the content of each major clinical department during the course of the subject committee teaching in the first two years. Although not required, it is anticipated that many students will take further clinical clerkships during the elective time available to them in the fourth year.

Free or Elective Time

As noted above, almost 50% of the student's time is subject to some degree of selection by him. During the first two years, three afternoons each week are completely unscheduled and available for his own pursuits. These may range from study, to research, to taking additional courses at the university, to recreation. At the end of the first year, one month of the basic medical sciences time has been set aside for elective courses which will permit stu-

dents in small groups to explore certain areas which they have found of particular interest. There will be two 3-month vacation periods, one at the end of the first year, and one at some time during the third year, during which some students will undoubtedly participate in independent research or in community activities. In addition, during the third year each student will engage in an individual project with a faculty member for three months; this may be in laboratory research, clinical research, community activity, or as a library project. Finally, during six months of the fourth year, the student will be completely free to develop an educational program most consonant with his own career goals and interests. Some students may spend the entire period in a single area; others may use it for a series of clinical clerkships. As was noted in the introduction, with special planning the exceptional student may find it possible to complete a traditional curriculum in three years and have a continuous period of the final twelve consecutive months available for his own planning.

Establishment of an Educational Milieu

In its efforts to develop a proper climate for learning and a primary emphasis on the educational process, the faculty has taken several steps. An early development was the creation of a faculty group known as the Committee on Educational Environment which developed policy proposals concerning the evaluation system, the nature of faculty-student interrelationships, and other matters which have an influence on the climate of an institution and the attitudes of students. One of its first recommendations was that there be developed within the Health Center a Department of Research in Health Education which would carry on both independent research in the field of education and be of assistance to the faculty in the development of the educational program. Dr. Edwin F. Rosinski has been appointed chairman of this department, coming to the institution after a long career in educational research at the Medical College of Virginia and immediately following two years as Deputy Assistant Secretary of Health, Education, and Welfare for Health Manpower. His department will assist the faculty in defining educational objectives, in developing pedagogic methods, and in evolving better means of evaluation of student performance.

Policy on Evaluation

The faculty has adopted a number of policies

concerning evaluation which should permit the utilization of evaluation procedures as a means of reinforcing teaching and as a means of continuous monitoring of student performance for purposes of continued guidance in the development of careers. Efforts are being made to develop methods of assessment in addition to traditional examinations, since many aspects of performance critical to effective professional performance cannot be measured simply by written examination. There will be several written examinations through the first year, but these will be primarily for self-assessment as practice exams. Although they will be graded, they will not count for promotion if a student passes a comprehensive examination at the end of the first and second years. Should he fail a comprehensive examination then prior adequate performance on the interim exams will serve to his benefit.

To reduce overemphasis on numerical examination grades and the intense competition frequently seen among students, all examinations are taken anonymously, no grades are posted, and no numerical grades are awarded. Rather, the students receive the general designation of "Satisfactory" or "Unsatisfactory", with outstanding performance being awarded "Honors". This de-emphasis on numerical grades and competition for rank in class has already been reflected in a change in student attitude. An environment inventory administered to the students at the beginning of school and at the end of eight weeks revealed a definite increase in students' feeling that their classmates were more colleagues than competitors.

Student Participation

Although there has been much national movement to include students in institutional policy-making as a symbolic gesture to their rights as consumers, there are two more significant reasons why the faculty at the University of Connecticut has invited participation of students both in setting policy and in developing operational programs. First, such participation adds significantly to the students' educational process itself; and second, the students have meaningful contributions to make in both policy and program development. Beginning with the first class this year student representatives sit as voting members of the General Faculty and as regular members of the several appointed committees of the General Faculty which deal with policy matters; namely, the Committee on Educational Environment which formulates the evaluation policy of the institution, the Committee on

Student Affairs which determines both admissions and promotions criteria, and the Committee on Undergraduate Medical Education which is responsible for development of specific curriculum proposals. Students participate in the actual development of the curriculum both by sitting on the subject committees which are responsible for developing individual segments of the curriculum and in being consulted regularly by the Associate Dean for Medical Education for a formal critique of each subject committee upon its completion.

By these several means continuing and open dialogue has been initiated between the faculty and student body to the better understanding of the goals, aspirations, and needs of both groups.

Summary

The University of Connecticut has developed what it believes to be a pedagogically sound and flexible curriculum designed for the education of

physicians who will enter increasingly diverse careers which will extend well into the next century.

The program is based on educational goals from which both the organizational framework and actual curriculum have derived directly. "Basic" or required experiences in both preclinical and clinical areas occupy approximately one-half of the available time so that there can be a major degree of election by the student. An effort has been made to evolve an educational environment where the major emphasis is on learning and individual effort. This has required development of a mature approach to the evaluation of student performance which is necessary both for professional accreditation and proper career guidance. General Faculty responsibility for educational policy and increasing participation by students in planning have added significant dimensions to assure continued evolution of the program to meet the changing needs of society.

MD-Astronaut

America's first astronaut-physician will be put into orbit around earth sometime in 1971, according to a time-table announced by an official of the National Aeronautics and Space Administration.

John Discher, deputy director of the program, which is called Apollo Applications, says four medical doctors are in the running to make the initial flight, which will be a 28-day space stay with two other men.

This flight, he said, would be to set up a space station. Another 28-day orbital flight to the station is planned for the purpose of medical experimentation.

A third flight, calling for 56 days in orbit, will be made to gain information on extended stays.

Inflammation—Leukocytes and Chemotaxis

Peter A. Ward, M.D.

Whatever happens to be his particular area of interest the practicing physician is constantly reminded of the importance of the inflammatory process. To the surgeon, the onset of the inflammatory process in the surgical wound heralds the complex series of changes leading to repair, healing and regeneration. The internist knows that, as fever and leukocytosis appear in a patient with a recent myocardial infarct, so also does the inflammatory response develop around the dead or dying myocardium. He is well aware of the pre-eminent role of the inflammatory process, without which the damaged heart could not heal. On the other hand, the onset of the inflammatory process in a homotransplanted heart or kidney means trouble for both the patient as well as the surgeon, and inflammation in the joint of an individual with rheumatoid arthritis only exacerbates any damage already inflicted on that joint.

There are not many occasions in clinical medicine where it is necessary, or even desirable, to enhance the inflammatory response beyond what nature has already done. But certainly there are numerous occasions when it is imperative that the inflammatory response be dampened or ablated altogether. If this is to be done by chemotherapeutic means, it is highly desirable that we first understand why and how the inflammatory response occurs and then how it can be manipulated. Our studies dealing with inflammation have been of a rather fundamental nature, but already there are several examples where that information has meaningful clinical application. In this report I would like to review our work on leukocyte chemotaxis and to point out where we have been able to apply it to human diseases.

The Inflammatory Process—Cells and Proteins

It is well known that the acute inflammatory process involves the outpouring of both leukocytes (primarily neutrophils) and plasma proteins from the circulation into extra-vascular sites. The proteins probably seep through walls of the capillaries and veins following the permeability increasing action of certain host mediators which include vaso-

active amines (histamine and serotonin) from mast cells and platelets, anaphylatoxins from the third or fifth components of complement, prostaglandins, and the kinins (see review, 1). But in addition to the escape of plasma proteins, the circulating leukocytes, first neutrophils and then mononuclear cells, begin to pour out of vessels during the acute inflammatory response. There have been some excellent electron-microscopic studies showing the transmigration of neutrophils, as they squeeze through tight junctional zones between endothelial cells to emerge on the outer aspect of the vessel.² What has become quite clear in the last decade is that increased vascular permeability and emigration of leukocytes are not necessarily synonymous. In the edema developing immediately after injury to soft tissue, especially around a joint, or in the wheal that follows a mosquito bite, there is extensive outpouring of plasma proteins, water and electrolytes, but very few leukocytes manage to escape from the circulation. From these observations, and many more, one is forced to conclude that factors controlling permeability are not necessarily those that determine leukocyte emigration.

Figure 1 shows the vessel of an animal with experimental immunologic vasculitis, induced by interaction of antigen, antibody and complement in the wall of the vessel. This picture was taken early (about 2 hrs.), before extravasation of red cells. There has been a heavy concentration of neutrophils both in and beyond the wall of the vessel. It is the presence of these leukocytes with their battery of destructive enzymes that leads to serious structural and functional damage to the vessel. It is because of the inflammatory response that tissue injury has occurred. The role of the immune reactants has been, quite simply, to trigger the inflammatory reaction. In the absence of leukocytes (neutrophils), for whatever cause, the vessel is spared the injury. In this report we will look into factors which may account for the accumulation of leukocytes in this and in similar reactions.

Chemotaxis

One of the more recent approaches to an understanding of leukocyte behavior in the inflammatory response has been the study of chemotaxis of leukocytes (leukotaxis) in vitro. *Chemotaxis* can be defined as the specific and unidirectional migration of

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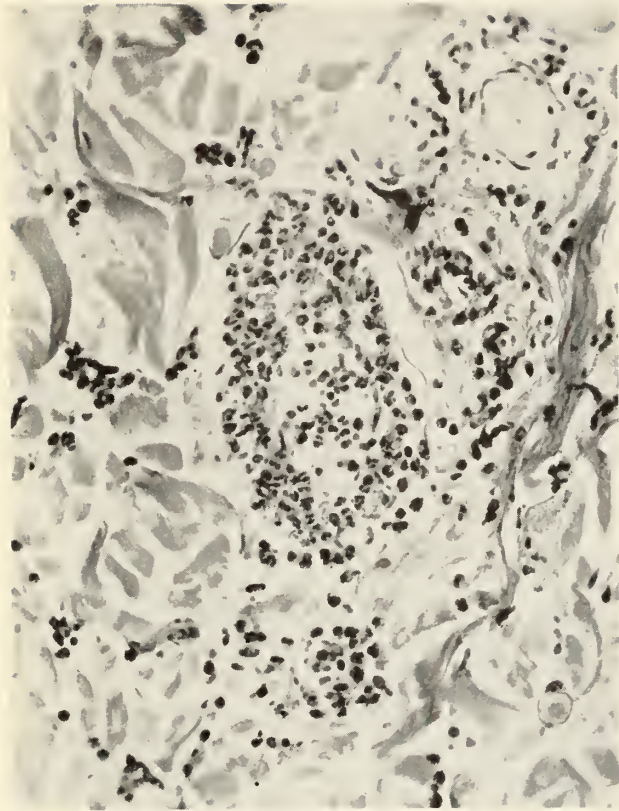


Figure 1

Histologic section of immunologic vasculitis (experimental). Numerous neutrophilic leukocytes have migrated out of the lumen of a venule and into its wall where they form a dense band. The escape of these leukocytes leads to destructive inflammatory injury of this vessel. Characteristically, the thicker-walled arteriole (upper right) is spared. Hematoxylin and eosin $\times 500$.

leukocytes towards an increasing concentration gradient of attractant. This subject has a long and tortured history, primarily because the techniques for the study of chemotaxis have been so crude as to preclude quantitation of cell migration. In 1962, Stephen Boyden in Australia introduced a revolutionary method for the study of leukotaxis.³ He employed a chamber with a micropore filter which would allow the migration of neutrophils only if a chemotactic factor was present in the compartment opposite the one containing the leukocytes. Probably the most important aspect of Boyden's technique was that the numbers of migrating cells could be assessed, thus providing a more precise quantitative aspect to the methodology. The micropore filter technique is now being used by several groups in and out of the United States, and it would appear that we are now into a new era of leukocyte chemotaxis.

It seems probable that the study of factors capable of causing the migration of leukocytes *in vitro*

will provide the basis for an understanding of leukocyte migration *in vivo*. With this in mind we can ask: (1) What are the factors able to induce leukocyte chemotaxis *in vitro*? (2) What is the nature of the interaction of the chemotactic factor and the leukocyte? (3) What is the role of chemotactic factors *in vivo*? (4) How can this knowledge be applied to clinical medicine?

By the use of micropore filters, it is possible to place granulocytes (neutrophils) on one side of the membrane and the putative chemotactic factor on the other side. Neutrophils will respond to the appropriate factor by migrating through the pores of the filter which, after removal, is stained and the numbers of migrating cells quantitated by light microscopy. So far, our studies have been confined to neutrophils and mononuclear cells which, by definition, may include macrophages, monocytes and lymphocytes. Substantial data have been accumulated dealing both with the chemotactic factors and the manner in which they cause the cell to crawl.

Factors Chemotactic for Neutrophils

Neutrophils are attracted by *soluble bacterial factors* and by a variety of reaction products generated from the complement system in plasma. Bacterial chemotactic factors have been found in most culture filtrates of bacteria, the exceptions being meningococci and a single tested strain of *Mycobacterium tuberculosis*.⁴ These chemotactic factors are substances, possibly peptides, produced during the replicative cycles of bacteria and are elaborated into the culture medium. Behaving in gel filtration like substances of low molecular weight (approximately 3,000), the factors require serum neither for their production, nor for the expression of chemotactic activity.

Complement Factors

In contrast to the chemotactic factors elaborated by bacteria, there are at least three factors chemotactic for neutrophils that require one or up to 7 of the 9 complement components present in serum. The complement system, consisting of 9 activities (i.e., 9 entities that participate in the hemolytic sequence required for lysis of sensitized erythrocytes), provides a source for 3 neutrophil chemotactic factors. Sequential interaction of the first 7 components leads to activation of the trimolecular complex, C₅₆₇, which consists of the fifth, sixth and seventh components of complement. C₅₆₇ acquires chemotactic activity for neutrophils as a result of triggering of the complement system by

such agents as antigen-antibody complexes.^{5, 6} It is now known that two other factors with chemotactic activity for neutrophils can also be generated from the complement sequence, each of which has been identified as a fragmentation product of a complement component, one from the third component (C3), the other from the fifth component (C5) of complement. The C3 fragment can be cleaved by the action of plasmin, thrombin and, possibly, trypsin.⁷ The C5 fragment appears after interaction of the first 5 complement components^{8, 9} or by the direct action of trypsin on C5.⁸ In addition, C3 can also be cleaved into a chemotactic fragment by a tissue protease present in the heart, lungs, spleen and liver.¹⁰

Chemotactic Factors in Animals and Man

All factors found to be chemotactic *in vitro* for neutrophils have been tested by intradermal injection into rabbits, and, in each case, the factor has caused the accumulation of large numbers of neutrophils at the site of injection. This has suggested that the *in vitro* activity of each factor is associated with corresponding biologic activity *in vivo*. Quite another approach to the problem of biologic activity has also been used. We have looked for chemotactic factors in the plasma or in exudates of animals or humans where there has been some reason to suspect that such factors might indeed be present. In experimental animals it has been possible to demonstrate a chemotactic factor, probably C567, circulating in the plasma after artificial activation of the complement sequence.⁶ As might be expected, this factor appears only transiently in the circulation—within 30 min. it is gone. Apparently the body has very efficient homeostatic mechanisms for ridding the body of mediators that initiate the inflammatory reaction. As for man, synovial fluids from patients with acute rheumatoid arthritis have been found to contain the complement associated chemotactic factor, C567.¹¹ It is of interest that these joint fluids characteristically contain large numbers of neutrophils, and the complement levels in these fluids, contrasted to normal synovial fluid, are very low. By immunoelectrophoresis the joint fluids reveal changes in β 1C globulin (C3) that suggest the complement system has been triggered. In collaboration with Dr. Nathan Zwaifler of the Georgetown University Hospital, we have found the presence of C567 in nearly two-thirds of all joint fluids from rheumatoid patients so far studied. Fluids from normal joints and from those of patients with osteoarthritis do

not contain this factor. To date no fragments of C3 or C5 with chemotactic activity have been found in rheumatoid joint fluids, but the very short biologic half life of these fragments complicates the search for them. As for the role of C567 in rheumatoid arthritis, it seems possible that in the joint fluids the complement system is somehow activated, resulting in the generation of C567. This factor is chemotactic for neutrophils and will cause the outpouring of neutrophils from synovial vessels, resulting in a joint fluid that contains cells with a high content of potentially destructive enzymes. With large numbers of neutrophils in the joint space some of the leukocytes inevitably begin to break down, either by cell death or enzyme discharge following phagocytosis of rheumatoid factor-complex. The end result is a joint that becomes bathed in enzymes that will damage or destroy its very structural elements.

It now seems reasonable to conclude that the complement system is very important for the induction of many inflammatory reactions. The isolation of numerous bioactive products from the various complement components indicates that the complement system is in fact a reservoir of substrates for the generation of a variety of phlogistic factors; each of these factors seems capable of inducing an acute inflammatory response. As has been pointed out, some of these mediators can be derived from complement components following the sequential interaction, in a cascade fashion, of successive complement components. Probably just as important, many of the bioactive products can be derived from reactions that bypass all but one complement component. In this way, plasmin can work directly on C3 and trypsin directly on C5 to generate chemotactic factors. It now seems likely we are going to find that more phlogistic factors from the complement system are produced in the bypass system (where only one complement component is utilized) than in the sequential reaction (that requires 4-9 of the components). If this indeed proves to be the case, the past emphasis on the immunologic role of the complement system might suddenly become inappropriate and represent a historical accident.

Enzymes in the Neutrophil Required for Chemotaxis

The fact that chemotactic factors can cause neutrophils to respond in a specific migratory manner implies that an interaction between the leukocyte and the factor has occurred. Recent studies indicate that C567 requires the functional interplay of two

esterases within the neutrophil if that cell is to respond chemotactically.¹² One esterase termed the "activatable esterase" exists in or on the neutrophil as a proenzyme, and contact of the cell with C567 leads to "activation", or conversion, of this enzyme to its active form.¹² This esterase appears to have an affinity for aromatic amino acid esters.¹³ A second esterase, termed the "activated esterase", is present continually in the cell as an active enzyme, and therefore, is constantly susceptible to inactivation by appropriate enzyme inhibitors. The activated esterase has an affinity for acetate esters.¹⁴ Although the metabolic requirement of these two esterases in the chemotactic response of the neutrophil has been documented, we have very few hints as to the real role of these enzymes in cell migration (chemotaxis).

Clinical Chemosuppression of Chemotaxis

What is the relevance of these experimental data to clinical medicine? To be sure, much of its direct relevance is, for the moment, obscure. If it were possible to find an enzyme inhibitor that would block in a highly specific manner one or both of the esterases in the neutrophil necessary for chemotactic responsiveness, then we would have an exquisitely specific antiphlogistic agent. Unfortunately, no such agents are yet available. On the other hand, we are now in a position to understand how certain drugs modify the inflammatory response. The study of neutrophil chemotaxis has lent itself to an understanding of the action of the anti-inflammatory drugs, namely, corticosteroids and chloroquine. These drugs have been used for several years in systemic lupus erythematosus and a variety of other inflammatory diseases, but their mechanisms of action have not been clearly understood. Recently we have found that hydrocortisone, methylprednisolone and chloroquine are very potent inhibitors of the chemotactic responsiveness of neutrophils.¹⁵ That is, these drugs in doses of about 10^{-5} M render neutrophils unresponsive to chemotactic stimuli. Attempts to induce acute immunologic vasculitides in animals pretreated with these drugs have failed, presumably due to the inability of circulating neutrophils to migrate out of vessels in response to locally produced chemotactic factors. Of course, this does not preclude other ways by which these drugs may work to prevent the inflammatory response, but at least there is a firm basis for postulating the suppressive activity in chemotaxis, and thus the anti-inflammatory nature of these drugs.

Mononuclear Cell Chemotaxis

Mononuclear cells, that is to say monocytes and phagocytes, have also been studied for their chemotactic responsiveness, and it is evident that these cells respond more sluggishly than neutrophils, since they require about 5 hours to complete their response compared to 1½ hours for neutrophils.¹⁶ Like neutrophils, mononuclear cells respond chemotactically to soluble bacterial factors and, probably, to the plasmin cleavage product of C3.¹⁶ On the other hand, mononuclear cells respond to a factor in serum that has been pretreated with immune complexes. The nature of this factor is not known, but there is firm evidence to say it is not associated with the complement system. Additionally, and most interestingly, mononuclear cells respond chemotactically to factors contained within the neutrophil. These neutrophil factors are not well defined but their recognition suggests that in some inflammatory exudates which contain neutrophils there is automatically present the stimulus to attract mononuclear cells. In this sense, then, it would be possible to explain the frequent appearance of monocytes following the arrival of neutrophils in an exudate.

The information on the neutrophil-contained factor that is chemotactic for mononuclear cells may explain why, in cases of cyclic neutropenia in humans, there are no mononuclear cells appearing in exudates at a time when the neutrophil count in the blood has fallen. The return of mononuclear cells in the exudates could be predicted when the neutrophil count returns to normal, and this in fact is exactly what is seen clinically.¹⁷

Mononuclear cells contain at least one esterase that is required for their chemotactic responsiveness, and this enzyme seems clearly different from either esterase found in the neutrophil.¹⁶ That the enzymes in the two cell types are not similar comes as no surprise in view of the known biochemical differences between mononuclear cells and neutrophils.

Conclusion

The studies on chemotactic mechanisms of leukocytes have provided us with a new outlook into the functional behavior of these cells as they are carried throughout the blood stream. We know the identity of a few of the chemotactic factors which are seemingly able to cause the migration of leukocytes beyond the confines of vessels, and we can detect the barest hints of interactions between these attractant factors and their target leukocytes. While only a few of the data listed in this report have

immediate clinical relevance, at least we have made a start in an understanding of factors controlling the inflammatory response. Further pursuit of these approaches offers promise of providing the physician with a more potent armamentarium for one control of destructive inflammatory processes.

Bibliography

1. Kellermeyer, R. W., and Graham, R. C., Jr. 1958. Kinins—possible physiologic and pathologic roles in man. *N. E. J. Med.* 279: 754.
2. Marchesi, V. T. 1964. Some electron microscopic observations on interactions between leukocytes, platelets, and endothelial cells in acute inflammation. *Ann. N. Y. Acad. Sci.* 111: 774.
3. Boyden, S. 1962. The chemotactic effect of mixtures of antibody and antigen on polymorphonuclear leukocytes. *J. Exp. Med.* 115:453.
4. Ward, P. A., Lepow, I. H., and Newman, L. J. 1968. Bacterial factors chemotactic for polymorphonuclear leukocytes. *Am. J. Path.*, 52:725.
5. Ward, P. A., Cochrane, C. G., and Muller-Eberhard, H. J. 1965. The role of serum complement in chemotaxis of leukocytes in vitro. *J. Exp. Med.*, 122:327.
6. Ward, P. A., Cochrane, C. G., and Muller-Eberhard, H. J. 1966. Further studies on the chemotactic factor of complement and its formation in vivo. *Immunology* 11:141.
7. Ward, P. A. 1967. A plasmin-split fragment of C'3 as a new chemotactic factor. *J. Exp. Med.* 126:189.
8. Ward, P. A., and Newman, L. J. 1969. A neutrophil chemotactic factor from human C'5. *J. of Immunol.* 102. (In press).
9. Shin, H. S., Snyderman, R., Friedman, E., Mellors, A. and Mayer, M. 1968. Chemotactic and anaphylatoxic fragment cleaved from the fifth component of guinea pig complement. *Science* 162:361.
10. Hill, J. H., and Ward, P. A. 1969. A neutrophil chemotactic factor from complement (C3) produced by a tissue protease. *Fed. Proc.*, 28:485.
11. Ward, P. A., and Zwaifler, N. J. 1968. Chemotactic factors for neutrophils in synovial fluids in rheumatoid arthritis. *Clin. Res.*, 16:325.
12. Ward, P. A., and Becker, E. L. 1967. Mechanisms of the inhibition of chemotaxis by phosphonate esters. *J. Exp. Med.*, 125:1001.
13. Ward, P. A., and Becker, E. L. 1968. The deactivation of rabbit neutrophils by chemotactic factor and the nature of the activatable esterase. *J. Exp. Med.*, 127:693.
14. Becker, E. L., and Ward, P. A. 1967. Partial biochemical characterization of the activated esterase required in the complement dependent chemotaxis of rabbit leukocytes. *J. Exp. Med.*, 125:1021.
15. Ward, P. A. 1966. The chemosuppression of chemotaxis. *J. Exp. Med.*, 124:209.
16. Ward, P. A. 1968. Chemotaxis of mononuclear cells. *J. of Exp. Med.*, 128:1201.
17. Page, A. R., and Good, R. A. 1967. Studies on cyclic neutropenia. *Am. J. Diseases Children*, 94:263.

When Is An Anecdote?

To be told by a friend that one's paper is merely anecdotal is to be rated very low indeed. One gets a mental picture of middle-aged or elderly colleagues, eagerly recounting tales of their childhood and youth or other personal reminiscences only vaguely connected with medicine. Yet the question when is an anecdote not an anecdote needs some thought.

The Greek word anecdote means something unpublished; and so all editors hope that everything they receive for publication is anecdotal. The English word has become, according to the *Shorter Oxford Dictionary*; "1. Secret, or hitherto unpublished narratives or details of history. 2. The narrative of an interesting or striking incident or event. (At first, an item of gossip)." . . .

It may be that people are suspicious of the anecdote since its content cannot be presented statistically. Or perhaps they are apprehensive that they will be accused of anecdotage. Yet even this word is old, if not venerable; for the Oxford Dictionary says the word first appeared in 1823.—Nathan, P. W.: When Is An Anecdote? *Lancet* 2:607 (Sept. 16) 1967.



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THE PRESIDENT'S PAGE

The efforts of American physicians to avoid being regimented by government, either directly or indirectly, continue to be challenged by a variety of politico-socio-economic forces. There is nothing new about this. It has been going on for more than three decades. Public officeholders, prominent labor leaders and their followings of somewhat misguided citizens, with the frequent aid of the news media and those who write for profit, are pressing their attacks on Medicine relentlessly, and we have no alternative but to step up our own programs designed to make our positions clear to all who will listen.

As of this writing, on the 10th day of May, not even a crystal ball could tell us what the outcome will be of the myriad health bills now pending in the Congress and in Connecticut's General Assembly. At all levels, the leadership of the profession has been active legislatively—evaluating the bills, developing reasoned positions on them, and presenting arguments in support or opposition in the most convincing manner possible. Your officers, members of our legislative committees and a number of dedicated CSMS members-at-large have given freely of their time and energies to go to Hartford—and even to Washington—to “bear witness” on behalf of their colleagues.

We have given support to bills which would: restore the “usual and customary charge” method of payment to the state's Medicaid program; retain in the Health Department the authority to inspect physicians' offices with regard to controlled drugs; create insurance pools to underwrite malpractice coverage for physicians and others; make legal the telephone prescribing of Class A narcotics in emergencies; establish health education as an integral part of public school curricula; legalize therapeutic abortion for carefully documented medical indication; make confidential the proceedings of hospital tissue committees and similar committees; and several other measures.

We have also vigorously opposed a few, examples: a bill to redefine the practice of optometry in such a way as to permit optometrists to practice ophthalmology; a bill to authorize the establishment of lay-controlled, tax-subsidized “health care centers” throughout the state; a bill to allow podiatrists to prescribe systemic drugs like narcotics and antibiotics.

As I said earlier, the fate of most of these measures is still in doubt. Everyone loves a winner, so it is claimed, and we who practice medicine would certainly like to achieve as many of our major legislative goals as possible—goals which we believe to be as much or more in the public interest as in our own. It is probable that we will lose out on some, too.

It is understandable that *all* of our members might not give their personal endorsement to *all* of the positions the Society has taken on the bills I have touched on and/or others that, in the interests of brevity, I failed to mention. Be that as it may, I believe that the cumulative efforts of all concerned with the implementation of our legislative program deserve great commendation, not only for the dedication with which these colleagues carried out their assigned duties but also for the dignified and responsible manner in which they tried to represent their fellow physicians before the representatives of the people. As your president, I extend my heartfelt thanks to every one of them.

STEVENS J. MARTIN, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

WILLIAM R. RICHARD, M.D. *Executive Director*

Peter F. Villano
Director of Public Relations

160 St. Ronan Street, New Haven, Conn. 06511
Telephone 865-0587

Josephine P. Lindquist
Associate Executive Director

SUMMARY OF ACTIONS COUNCIL MEETING

Thursday, April 17, 1969

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Gardner, Grendon, Weber, Jr., Brandon, Abbot, Dean, Bradley, Cramer, Farrell, Egan, Petrie, Shepard, J. M. Grant, Nemoitin, Johnson, Friedberg, McDonald, R. F. Grant, Pelz, Granoff, Palomba and Roch.

Also present were: Mrs. Lindquist, Dr. Patterson, Dr. Hess, Dr. Goldstein, Mr. Donelan (AMA), Mr. Villano and Dr. Richards.

Absent were: Drs. Fabro, Rogol, Spitz, Purnell and Wilson.

II. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following Active Members:

John P. Bachman, Newington (HCMA)—1969

E. Roland Hill, Mystic (NLCMA)—1969

Benjamin Horn, Bridgeport (FCMA)—1969

Michael E. Vegilante, New Haven (NHCMA)—1970

W. Bradford Walker, Cornwall (LCMA)—1970

CSMS Dues Exemption

It was VOTED to exempt from payment of CSMS membership dues the following Active Member for the indication and period stipulated:

Gert M. K. Wallach, Torrington (LCMA)—Post-graduate Education—1969.

Date of Next Meeting

The Chairman was authorized to call a meeting of the Council, if necessary, prior to the annual meeting of the House of Delegates, May 13-14, 1969. Otherwise, the President will call the next meeting "as soon as possible" after the meeting of the House.

III. Old, New and Special Business

Consolidated Actions of Council

and House of Delegates, 1957-1968

Kenneth F. Brandon, Hartford, submitted a report which represented a gathering, correlation and consolidation of all significant actions taken by the Council and House of Delegates during the

period January, 1957-December, 1968, and indexing same chronologically and by categories. It was VOTED to approve the report, with great commendation, and to extend to Dr. Brandon the Council's appreciation of a monumental job well done. It was similarly VOTED to thank and commend Mrs. Lindquist and her staff assistant, Mrs. Kinney, for the excellence of their work in locating the subject actions from the official records and excerpting them for Dr. Brandon's study and organization.

Finally, it was VOTED to furnish a copy of this report, along with a revised copy of the CSMS By-laws, in a suitable folder, to each member of the 1969 House of Delegates and to the presidents and secretaries of the component County Medical Associations; and to direct that the index be updated currently and republished every three years.

Report on 3rd National Congress

on Socio-Economics of Health Care

It was VOTED to receive as information, and with commendation, a report on the proceedings of this Congress, filed by James H. Root, Jr., Waterbury, who attended as a representative of the Society. Dr. Root is Chairman of the CSMS Committee on Third Party Payments. It was further VOTED to direct the Public Relations Director to interview Dr. Root on this subject, and to publish the interview in an issue of *Connecticut M.D.* for the information of the general membership. Copies of the report are being distributed to the members of the Third Party Payments Committee for study and discussion.

Report on AMA-ABA National Medical-Legal Symposium

It was VOTED to receive as information, and with commendation, a report on the proceedings of this Symposium filed by J. Alfred Fabro, Torrington, who attended as a representative of the Society. Dr. Fabro is Chairman of the Conference Committee with the State Bar Association and of the Judicial Committee. It was further VOTED to act on a series of recommendations accompanying the report as follows:

(a) That implementation be authorized, at the next feasible meeting of the Society, of a pro-

posal to arrange and conduct a program for the general membership on subjects of interest to physicians in the field of medico-legal medicine.

- (b) That approval be given to having a member of the Conference Committee with the Bar Association meet with a legal representative of the Aetna Life Insurance Co., on a personal and informal basis, to discuss various aspects of malpractice insurance and the increasing problems currently associated with same, and that Dr. Fabro be designated as the member of the Conference Committee to engage in such discussion.
- (c) That Kurt Pelz, Wallingford, President of the New Haven County Medical Association, be asked to arrange for an informed member of that Association to join the Council at a mutually convenient future meeting to present a succinct outline of the method by which the New Haven Association handles malpractice suits against its members or threats of same; also, a summary of the Association's experience with such cases in recent years. If deemed appropriate by the NHCMA member presenting this information, printed material on the subject will be welcomed by the Council.

Report—AMA 15th Annual Conference of State Mental Health Representatives

It was VOTED to accept as information, and with thanks, a report on the proceedings of this Conference filed by Frederick J. Flynn, Jr., Hartford, who attended as a representative of the Society. Dr. Flynn is a member of the CSMS Committee on Mental Health. Copies of the report will be distributed to all members of the Committee.

Request—Connecticut Hospital Planning Commission, Inc.

The Council was advised that the CHPC has been requested to undertake a study of the obstetrical facilities in hospitals throughout the State with the objective of determining which of these facilities may be unnecessary or being operated inefficiently and/or at too great cost, and to make recommendations concerning same. To take part in the study, the CHPC is forming a "Technical Advisory Committee" and requests that the Council recommend qualified members (about 6-8) to serve on the TAC and contribute their expertise to the study. In response to this request, the Council VOTED to designate Stewart J. Petrie, Derby, as a Committee of One, in consultation with the Chairmen of the CSMS Committee on Hospitals and the Section on Obstetrics and Gynecology, to formulate a panel of such qualified members to

submit to the CHPC at the earliest time possible. It was further VOTED to ask Dr. Petrie to inquire as to what the total membership of the Task Force was planned to be and to make a recommendation to the CHPC concerning the percentage of CSMS-designates that he would feel to be appropriate.

Communication—Commissioner, Department of Correction

Having received a request from Commission Ellis C. MacDougall, State Department of Correction, that representatives of the Council meet with him to discuss "longrange planning of medical services" for the Department and the possible formation of a "Medical Services Advisory Board" to assist in the development of such plans, the Council VOTED to ask Edward A. Palomba, Somers, and James M. Grant, Westport, to meet with Commissioner MacDougall for these purposes.

Report—Committee on Cooperation with Medical Schools of Connecticut

It was VOTED to receive as information, and with thanks, a report of this Committee, filed by Edward Nichols, Hartford, Chairman. It was further VOTED to act on two recommendations made by Dr. Nichols as follows:

- (a) *The Nomination of Medical School Faculty Members to CSMS Committees:* To advise Dr. Nichols that, pursuant to his recommendation, a number of faculty members at the Yale and UConn Medical Schools (who are members of the Society) have been nominated by the Council for CSMS committee service in 1969-70 and will be up for election by the House of Delegates on May 13-14, 1969. Having been apprised that a large number of medical school faculty members (especially at Yale) are not members of the Society, it was further VOTED to ask the Committee, in consultation with Dean Redich and Dean Patterson, to study and make recommendations concerning ways and means of increasing CSMS membership among such faculty personnel.
- (b) *Liaison with Medical Student Groups:* To authorize the Committee to establish liaison with medical school student groups with engage in activities of various kinds, in cooperation with medical school officials in charge of student affairs, to the end that practicing physicians and other CSMS representatives might contribute to the planning and implementation of student action programs.

COMPAC

- (a) It was VOTED to receive, as information, and with thanks, a COMPAC staff report on the COMPAC-CSMS Conference for County Medi-

cal Association Officers and Others which was held in New Haven on March 19, 1969.

- (b) It was VOTED to accept, with thanks, a report filed by the Council's Ad Hoc Committee to Study CSMS-COMPAC Relationships, and, as amended, to approve a series of recommendations which accompanied same. It was further VOTED to transmit to the House of Delegates, on May 13-14, 1969, the report and recommendations of the Council on this subject, and to recommend approval of same by the House. It is understood that the report, along with subject resolutions of the County Associations, will receive full discussion in a Reference Committee hearing before being presented to the House for final action.

Employment of an Assistant General Manager

Having reviewed an October, 1967 report of the Ad Hoc Committee on Administrative Organization and Planning, which outlined the prospective qualifications and duties of a person to fill the post of Assistant General Manager, the Council VOTED to move ahead in its quest for a qualified person to be employed in such a capacity and to direct the Chairman to update the roster of members of the Ad Hoc Committee and designate the chairman thereof, such Ad Hoc Committee to seek out qualified candidates, interview them, and make recommendations to the Council as to a specific person to be employed.

Medicaid—"Usual and Customary Charge"

- (a) Drs. Gardner and Richards reported on the April 11th press conference called by Commissioner Shapiro for the purpose of releasing to the communications media the names of all physicians who had received more than \$2500 in Medicaid payments during calendar 1968 (two months on fee schedule and ten months on "usual and customary") and the amounts paid to each; also, to release information concerning the amounts paid to hospitals, nursing homes and other providers of health services during the same period. In general it may be said that the Commissioner presented the information in a careful, detailed manner and gave explanations on all points which might have been subject to misinterpretation. In essence, it can be stated categorically that no "skeletons in the closet" were discovered and no "scandals" of any kind came to light. Save for the fact that the Society considers this sort of "three ring circus" to be an exercise in futility and a needless source of possible public

embarrassment to physicians, and has said so, it is clear that the Medicaid program as it operated from March 1, 1968-March 1, 1969 accomplished great things for the State's needy and near-needy and that the medical profession is entitled to kudos—not carping criticism—for the responsible role doctors have played in making those accomplishments possible. It was VOTED to accept these verbal reports as information .

- (b) Max Goldstein, Hartford, joined the Council to report on the progress which has been made by his Council-endorsed Ad Hoc Committee to restore the usual and customary charge concept to Medicaid in the coming biennium through appropriate legislative activity. The Council VOTED to approve the Ad Hoc Committee's proposal, in principle, and to approve its being promoted legislatively as an alternative to S. B. 574 if developments warrant.
- (c) It was VOTED to approve the draft of a letter composed by the General Manager which would apprise members of the Society of the current legislative situation with regard to the possible restoration of the "usual and customary charge" method of payment to the Medicaid program for the next biennium, and to urge them, to the fullest extent possible, not to change their present physician-patient relationship with Medicaid beneficiaries until they receive notice of the definitive action taken by the General Assembly and have an opportunity to determine whether any permanent change made in the program might adversely affect such relationships in the future. It was further VOTED to direct the staff to conduct a mailing of this letter to the entire membership.
- (d) The Council was also apprised that a spokesman for the Department of HEW has announced publicly that the Nixon administration has proposed regulations to become effective July 1, 1969, which, if approved by the Congress or not successfully contested by the providers of health services, would impose stringent controls on the payments made to such providers for services rendered to Medicaid beneficiaries. Insofar as physicians' services are concerned, the proposed regulations would limit charges to the "prevailing Blue Shield payment plans for non-government medical service"; i.e., that "usual and customary" could no longer be used. It was VOTED to request E. Tremain Bradley, Norwalk, Im-

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mediate Past President, to seek to arrange an audience with HEW Secretary Finch for himself, Dr. Gardner and Dr. Martin at the earliest possible time, and to seek the assistance of the AMA, Rep. Meskill and Rep. Weicker in making such arrangement. The purpose of the meeting with the Secretary would be to try to convince him that the application of such stringent controls would be disastrous to Connecticut's highly effective Medicaid program and would quite probably be fatal to the efforts of all concerned to bring first-class medical citizenship to the under-privileged.

Other Legislation

- (a) *Prescribing of Systemic Drugs by Chiropractors:* Isadore H. Friedberg, Chairman of the Committee on State Legislation, recounted his efforts and those of Commissioner Foote to convince the Assembly's Committee on Public Health and Safety that, in general, it is not in the public interest to permit chiropractors to prescribe systemic medications (such as narcotics and antibiotics). It is Dr. Friedberg's educated guess that the chiropractors may be given authorization to prescribe non-narcotic analgesics, but he is hopeful that authorization will be limited to such drugs.
- (b) *Authority to Inspect Physician's Office re Controlled Drugs:* Dr. Friedberg also brought the Council up to date on the controversy between the Department of Health and the Department of Consumer Protection concerning which of the two should have the authority to carry out the function of drug control through the inspection of pharmacies and physicians' offices. Consumer Protection, under whose jurisdiction the licensing of pharmacists lies, presently has the authority to inspect retail pharmacies—including examination of all stocks and records on narcotics and other controlled drugs. The State Health Department, under whose jurisdiction lies the licensing of hospitals, nursing homes and physicians, presently has the authority to inspect hospital and nursing home pharmacies and physicians' offices—including the subject examinations regarding drugs. There are two bills before the General Assembly—one (HB 6874) which would transfer *all* authority for drug inspections to Consumer Protection, and another (HB 6317) which would retain institutional pharmacies and physicians' offices under the Health Department's jurisdiction. Pursuant to a lengthy

discussion of this matter it was VOTED to take the following actions:

- (1) To encourage member contact with legislators to gain support for HB 6317.
- (2) To send a supporting statement to all members of the General Assembly and issue a press release on same.
- (3) To direct the President to arrange an audience with Governor Dempsey to urge his support of HB 6317, the President to be accompanied by the following volunteers: Drs. Martin, Bradley, Grendon, Pelz and Friedberg. (N.B.: In actual implementation, Dr. Martin arranged for a meeting with the Governor, but, at the Governor's request, limited the "delegation of CSMS representatives" to himself alone.)

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on April 17, 1969. Detailed minutes of the meeting are on file at 160 St. Honan Street, New Haven, for perusal by any interested member of the society.*

Placement Wanted

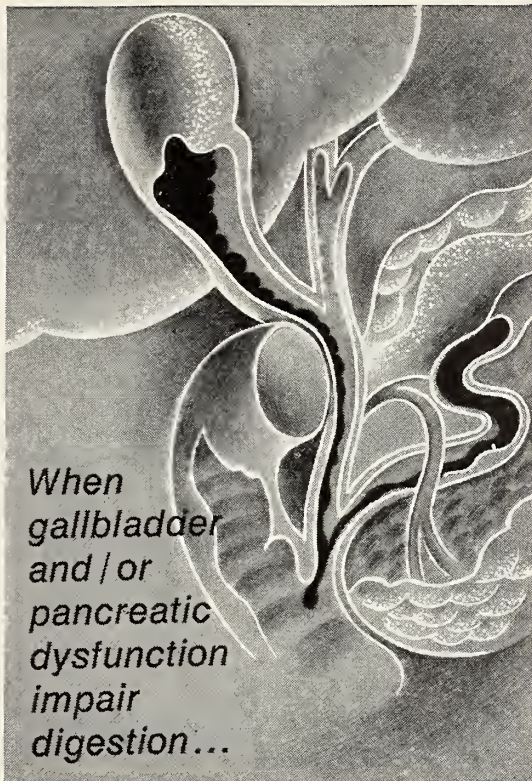
INTERNIST—33, Board eligible, subspecialty in Rheumatology, Connecticut license. Desires to locate in Connecticut and interested in practicing either in association, group, hospital, student or employee health. Available Summer 1969.

GENERALIST—Age 62, desires position in Connecticut full time, 40 hours per week in hospital or emergency room service, or employees' clinic in industry. Connecticut license. Available immediately.

DERMATOLOGIST—31, Board eligible, presently completing residency. Available July, 1969. Has National Boards. Desires solo or group or clinic-type practice. No present preference as to size of community.

INTERNIST—University trained, with special interest in Infectious Diseases desires private practice association with another Internist or group in Connecticut. Available on completion of military service, July, 1970, Early commitment is desired.

UROLOGIST—32, Married, completing residency. Board eligible, seeks interesting professional opportunity, preferably association.



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WANTED: Internist for General Medical and Surgical Accredited State Veterans Hospital. Duties are those of a ward officer on a general medical ward. Applicants must be Board eligible and up to 65 years of age, if still vigorous. Salary range: \$17,980-\$22,180. Many fringe benefits. Apply Personnel Officers, Veterans Home and Hospital, Rocky Hill, Connecticut.

PHYSICIAN for Emergency Room in 90 bed community hospital in Central Connecticut. 40 hour week, weekends free, if desired. Full cooperation from panel of staff physicians who cover E.R. remaining time. Must be eligible for Connecticut license. About \$30,000 per year. Reply: Joseph Zimmerman, M.D., P.O. Box 687, Meriden, Connecticut 06450.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Rutgers Offers Study in Alcoholism Field

Three special programs for persons working in or interested in the field of alcoholism are being offered by the Rutgers Center of Alcohol Studies this coming summer.

The three-week course program (June 29-July 18, 1969) is designed for caseworkers, clergymen, educators, public health workers and other professionals actively employed in some alcohol problem.

Prime purpose of the School is to help strengthen alcoholism and alcohol-related programs which now exist by training staff members—particularly those who make policy, train, supervise, do community organization or educating.

A second course program is the Physicians Institute which is open to holders of medical degrees, and is an integral part of the School. Classes will meet during the first two of these three weeks (June 29-July 11, 1969). Topics will include the etiology and clinical course of alcoholism, treatment of the acute stages, major approaches to therapy, and issues in program planning of alcoholism treatment facilities.

The Institute is co-sponsored by the official alcoholism programs of Connecticut, Maine, Maryland, New Jersey, New Hampshire, New York, Pennsylvania, Rhode Island and Vermont.

Because of their experience and expertise in the field, four Connecticut representatives will act as interdisciplinary group leaders during the Institute's program.

Group leaders from the Alcohol and Drug Dependence Division will be Donald J. Anneser, Education Director; Francis K. Hayes, Chief, Psychiatric Social Services; and Lillian L. Kendall, Director of Nursing. Walter A. Stewart, Director, Greater Hartford Council on Alcoholism will join to Alcohol and Drug Dependence Division group as an interdisciplinary leader.

All three programs will be held on the Rutgers University Campus. Tuition, room and board for the three-week Summer School or the Physicians Institute is \$325.00. Total cost for the Northeast Institute is \$110.00.

Announcement bulletins, official application forms and scholarship information may be obtained by writing to: Summer School of Alcohol Studies, or Northeast Institute of Alcohol Studies, Rutgers University, New Brunswick, New Jersey 08903. A limited number of applications are available from the Education Section, Alcohol and Drug Dependence Division, 51 Coventry Street, Hartford 06112.

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- David I. Campbell, M.D., 1389 West Main St. Waterbury, Conn. 06708.
- Claudio Crupi, M.D., 911 Country Club Road, Waterbury, Conn. 06708.
- Marshall Edelson, M.D., 34 Park Street, New Haven, Conn. 06519.
- Terence C. Feir, M.D., Griffin Hospital, Derby, Conn. 06418.
- John E. Fenn, M.D., 100 York Street, New Haven, Conn. 06511.
- Amir H. Hemmat, M.D. Undercliff Hospital, Meriden, Conn. 06450.
- Martin J. Kligerman, M.D., V.A. Hospital, West Haven, Conn. 06516.
- Lawrence F. McDonald, M.D., 333 Cedar Street, New Haven, Conn. 06510.
- Etsuro K. Motoyama, M.D., 333 Cedar Street, New Haven, Conn. 06510.
- Franklin F. Nejame, M.D., 173 Willow Street, Waterbury, Conn. 06710.
- Lance M. Osadchey, M.D., Meriden Hospital, Meriden, Conn. 06450.
- Robert R. Rickert, M.D., 310 Cedar Street, New Haven, Conn. 06510.
- John B. Schoonmaker, M.D., 377 Main Street, West Haven, Conn. 06516.

Fairfield County

- Harold Abrams, M.D., 881 Lafayette Street, Bridgeport, Conn. 06603.
- Paul Bachner, M.D., Greenwich Hospital, Greenwich, Conn. 06830.
- George A. Bullwinkel, Jr., M.D., 1911 Summer Street, Stamford, Conn. 06905.
- Ramona M. Byard, M.D., St. Vincent's Hospital, Bridgeport, Conn. 06606.
- Milton E. Campbell, M.D., 153 Mason Street, Greenwich, Conn. 06830.
- Melvin P. Coolidge, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.
- Martin Fox, M.D., 1425 Bedford Street, Stamford, Conn. 06905.
- William B. Goldstein, M.D., Cornell Road, Danbury, Conn. 06811.
- Edward A. Griffiths, M.D., 1 Atlantic Street, Stamford, Conn. 06901.
- Samuel R. Harrell, M.D., 1089 Post Road, Darien, Conn. 06820.
- Michael J. Kelleher, M.D., 2660 Main Street, Bridgeport, Conn. 06606.
- Neil C. Klein, M.D., 31 Strawberry Hill Avenue, Stamford, Conn. 06902.
- Claude F. Light, M.D., 494 Main Upper Street, Monroe, Conn. 06468.

- Forrest E. H. Lightbody, M.D., Greenwich Hospital Association, Greenwich, Conn. 06830.
- Eugene M. Marks, M.D., 939 Barnum Avenue, Bridgeport, Conn. 06602.
- Andrew G. Reitwiesner, M.D., Danbury Hospital, Danbury, Conn. 06810.
- Jerome S. Resnick, M.D., 125 Strawberry Hill Avenue, Stamford, Conn. 06902.
- Gaston E. Roy, M.D., Valley Road, New Canaan, Conn. 06840.
- Barry E. White, M.D., 50 Ridgefield Avenue, Bridgeport, Conn. 06610.
- Erwin Zingmond, M.D., 935 White Plains Road Trumbull, Conn. 06611.

Hartford County

- Burton N. Alter, M.D., 85 Jefferson Street, Hartford, Conn. 06103.
- Jonathan Berger, M.D., 477 Connecticut Boulevard, East Hartford, Conn. 06108.
- Austin R. Breneman, M.D., 85 Jefferson Street, Hartford, Conn. 06103.
- William R. Bronson, M.D., Hartford Hospital, Hartford, Conn. 06115.
- William A. Clarke, M.D., Connecticut General Life Insurance Company, Hartford, Conn. 06115.
- Robert T. Cosentino, M.D., Grove Hill Clinic, New Britain, Conn. 06050.
- Michael J. Dunne, M.D., 80 Doane Street, Manchester, Conn. 06040.
- Harvey I. Finkelstein, M.D., 100 Grand Street, New Britain, Conn. 06052.
- David M. Geetter, M.D., 287 Collins Street, Hartford, Conn. 06105.
- John Haksteen, M.D., 85 Jefferson Street, Hartford Conn. 06103.
- Brian C. Hennessey, M.D., 88 Goodwin Street, Bristol, Conn. 06010.
- Ned Hickmon, M.D., 140 Woodland Street, Hartford, Conn. 06105.
- Harry B. Hoffman, M.D., 85 Jefferson Street, Hartford, Conn. 06103.
- Malcolm L. Hunt, M.D., 151 Farmington Avenue, Hartford, Conn. 06115.
- Myron R. Hurwitz, M.D., 400 Washington Street, Hartford, Conn. 06106.
- Claude A. Lanctot, M.D., 79 Elm Street, Hartford, Conn. 06115.
- Edgar Lichstein, M.D., Grove Hill Clinic, New Britain, Conn. 06050.
- Ira H. Monosson, M.D., 201 Main Street, Southington, Conn. 06489.
- Charles E. Morhardt, M.D., 45 South Main Street, West Hartford, Conn. 06107.
- Edward E. Morse, M.D., McCook Hospital, Hartford, Conn. 06112.
- Robert Moss, M.D., 73 Cedar Street, New Britain, Conn. 06050.
- Manny Myerson, M.D., 106 Gillett Street, Hartford, Conn. 06105.

Donald Pet, M.D., Blue Hills Hospital, Hartford, Conn. 06112.
 Joseph P. Rossi, M.D., 79 Elm Street, Hartford, Conn. 06115.
 Ernest C. Shortliffe, M.D., Hartford Hospital, Hartford, Conn. 06115.
 Carolyn R. Sunderman, M.D., 139 Mountain Spring Road, Farmington, Conn. 06032.
 James M. Toomey, M.D., 2 Holcomb Street, Hartford, Conn. 06112.
 Harold F. West, M.D., 64 Maple Avenue, Collinsville, Conn. 06022.
 Richard N. Wilcox, M.D., 223 West Main Street, New Britain, Conn. 06052.
 H. Paul Winalski, M.D., 114 Woodland Street, Hartford, Conn. 06105.
 Richard V. Worrell, M.D., McCook Hospital, Hartford, Conn. 06112.

Litchfield County

Harry C. Briggs, M.D., 71 Spencer Street, Winsted, Conn. 06098.
 Rama P. Coomaraswamy, M.D., Hospital Hill, Sharon, Conn. 06069.
 Erly P. Gallo, M.D., 10 Hinsdale Avenue, Winsted, Conn. 06098.
 Edward B. McCabe, M.D., Winsted Memorial Hospital, Winsted, Conn. 06098.
 Charles S. Mirabile, Jr., M.D., 200 Retreat Avenue, Hartford, Conn. 06103.

Middlesex County

Richard J. Adams, M.D., 18 Crescent Street, Middletown, Conn. 06457.
 Anthony J. Arena, M.D., 195 South Main Street, Middletown, Conn. 06457.
 Edgardo Betancourt, M.D., 404 Congdon Street, Middletown, Conn. 06457.
 Daniel F. S. Crowther, M.D., 269 Main Street, Cromwell, Conn. 06415.
 Michael J. Lambe, M.D., East Street, Middletown, Conn. 06457.
 Fredric I. Fischbein, M.D., 40-35 Hampton Street, Elmhurst, New York 11373.

New London County

Malcolm S. Edgar, Jr., M.D., 2 Clinic Drive, Norwich, Conn. 06360.
 Robert F. Jones, M.D., 546 Williams Avenue, New London, Conn. 06320.
 Anthony K. Knirsch, M.D., 7 Plant Drive, Waterford, Conn. 06385.
 Thomas J. McGrath, M.D., 117 Lafayette Street, Norwich, Conn. 06360.
 Bruce H. Rice, M.D., Box 613, RFD #1, Gales Ferry, Conn. 06335.

Tolland County

W. Ames La Pan, M.D., Tolland Professional Building, RFD #4, Rockville, Conn. 06066.

Windham County

Joseph E. Bouthillier, M.D., R.D. 2 Pomfret Road, Putnam, Conn. 06260.
 Peter J. Calise, M.D., Windham Community Hospital, Willimantic, Conn. 06226.
 Luther W. Gibson, M.D., 132 Mansfield Avenue, Willimantic, Conn. 06226.

MEETINGS

GENERAL

July 13-17

118th Annual Convention, American Medical Association

Americana Hotel, New York City; Exhibits, Coliseum

AMA 53rd Annual Golf Tournament, will be held Thursday, July 14 at the Winged Foot Golf Club, Mamaroneck, N.Y. All AMA members are eligible to play; information may be obtained from J. H. Lebe, M.D., 120 Broadway, N.Y.

October 23

186th Semi-Annual Meeting, New Haven County Medical Association

Waverly Inn, Cheshire

Business Meeting, 3:00 P.M.; Social Hour and Dinner to follow.

BASIC SCIENCE

Recent Advances in Clinical Physiology

Lawrence and Memorial Hospitals, New London
 June 3 7:15 P.M.

Steroids, Growth Hormone, Growth Retardation
 Dorothea Hellman, M.D., Assistant Professor in
 Medicine Tufts University

June 10 7:15 P.M.

Newer Concepts of Graves Disease
 Dr. Hellman

MEDICINE

Wednesdays 12:00 P.M.-1:15 P.M.

Pulmonary Diseases and Pulmonary Physiology
 Radiation Center Conference, Room, Hospital of
 St. Raphael, New Haven

Chairman: John B. Berte, M.D., Director, Department of Pulmonary Diseases and Inhalation Therapy, Hospital of St. Raphael

Open to all physicians

Thursdays 1:30 P.M.-3:30 P.M.

Hematology

Hematology Laboratory and Wards, Hospital of
 St. Raphael, New Haven

Robert P. Zanes, Jr., M.D., Hospital of St. Raphael
 Open to all physicians

September 26-27

Regional Meeting (New England, Canada) of the
 American College of Physicians

Mary S. Harkness Auditorium, Yale Medical School

WOMAN'S AUXILIARY

President

Mrs. James F. Jones, Danielson

President Elect

Mrs. John J. Mendillo, Hamden

First Vice-President

Mrs. Noah Barysh, New Milford

Second Vice-President

Mrs. Joseph C. Czarsty, Oakville



Recording Secretary

Mrs. Melville Y. Alderman, West Hartford

Corresponding Secretary

Mrs. Stanley J. Weigel, Danielson

Treasurer

Mrs. Edwin R. Connors, Pawcatuck

The forty-sixth annual convention of the Woman's Auxiliary to the American Medical Association will be held in New York City, July 13-17, 1969 with headquarters at the Waldorf-Astoria Hotel. Registration will start Sunday, July 13 at 11 A.M. and continue through Wednesday, July 16 at 1 P.M. Meetings are open to all members and guests. We welcome all physicians' wives. However, only qualified delegates may introduce business or vote. The number of delegates from each state is determined by the paid membership as of March 31.

On Sunday evening the AMA Medicine and Religion Program will be held at the Americana Hotel with the subject—"Physician-Clergy Responsibility in Drug Abuse".

Monday's Keynote Address, "The Anthropologist Looks at Health in a Changing World", will be delivered by Ethel Alpenfels, Ph.D., Professor of Anthropology at N.Y.U.

The annual luncheon of the Auxiliary will be held on Monday, July 14 and Dr. Dwight L. Wilbur, president of the AMA, will be guest speaker. Presentation of the Auxiliary's annual contribution to AMA-ERF will be made at this luncheon. During the afternoon state auxiliary reports will be presented.

Presentation of AMA-ERF and AMPAC reports and several awards will be made on Tuesday, July 15. "Show and Tell" or demonstrations of exhibits developed by State and County Auxiliaries will be shown. At luncheon Ann Landers, Nationally Syndicated Columnist and member of the AMA Advisory Committee on Health Care of the American People will speak, her topic being "Is There a Doctor in the House?".

The general meeting will be held on Wednesday morning and will include the installation of officers and directors, and the inaugural address of Mrs. John M. Chenault.

For those taking their families to New York it is of interest that special pre-teen and teenage tours will be available each day of the convention. For pre-teens (6 to 12) these include tours of Little Old New York (historic Trinity Churchyard—Statue of Liberty—United Nations); Midtown Highlights (NBC studios—Lincoln Center—New York Police Academy); From the Past into Space (Museum of the City of New York—World of Tomorrow at the Allied Chemical Tower—Central Park Zoo—Empire State Building); Art and Amusement (Museum of Natural History of Metropolitan Museum of Art—Palisades Amusement Park); Dinner and Radio City Music Hall. The teenagers (13-17) will also have tours of Little Old New York, Midtown Highlights and Art and Amusement. They will have a Show Business and Science Tour (guest at top TV show or a backstage tour of a Broadway theatre—World of Tomorrow—Empire State Building); Night on the town (dinner in Chinatown—visit to Greenwich Village and the famed Bitter End—the top teen spot in town).

The American Medical Association has asked us to notify you that AMA registration and exhibits will open Sunday 10:00 A.M. (8:30 A.M. other days) and close Thursday at 5:00 P.M.—New York Coliseum. Tuesday, Wednesday and Thursday mornings at the exhibit hall will be limited to physicians, medical students and exhibitors only. Members of the Woman's Auxiliary may visit the exhibits at any other time. Admission will be by auxiliary badge.

OBITUARY

Anthony J. Loiacano, M.D.
1900-1968

Anthony J. Loiacano, M.D. died December 20, 1968 after a long illness.

Dr. Loiacano was born in New York City, October 24, 1900 and moved to New London at an early age. He graduated from Bulkeley High School in 1919 and attended Brown University from which he graduated in 1923. While at Brown he was Phi Beta Kappa, a John Manning Scholar, and a member of Sigma XI science fraternity. Dr. Loiacano graduated from Harvard University Medical School in 1927 and interned at Chester, Pennsylvania and Rhode Island Hospital, Providence, Rhode Island. He received his surgical training at Truesdale Hospital, Fall River, Massachusetts.

He practiced general medicine and surgery for thirty-six years with staff appointments at Lawrence and Memorial Hospitals, New London, Connecticut.

Dr. Loiacano was a Fellow of the American College of Surgeons, a member of the New London City, County Medical Society and the Connecticut State Medical Society. He was a member of the Thames Club and St. Joseph's Church in New London.

He was interested in bowling, saltwater fishing and bridge.

Dr. Loiacano is survived by his widow Ann Frauer Loiacano, two brothers, Richard Loiacano, M.D. and Albert, and three sisters.

John F. Brosnan, M.D.

In Memoriam

Bassin, Alexander L., New Haven, University of Rochester 1930. Dr. Bassin was an orthopedic surgeon in the New Haven area since 1931. He was a former chief of orthopedics surgery at Yale-New Haven Hospital and clinical assistant professor of orthopedics at medical school. He was attending orthopedist at the Children's Community Center, assistant attending surgeon of orthopedics at Yale-New Haven Hospital, and a attending orthopedic surgeon at St. Raphael's Hospital, New Haven and Griffin Hospital, Derby. Dr. Bassin was a commander in the U.S. Navy from 1943-46. He was a

member of the American Academy of Orthopedic Surgeons, the American Medical Association and the Connecticut State Medical Society. Dr. Bassin died on April 17 at the age of 65.

Dray, Edward J., New Britain, Jefferson Medical College 1909. Dr. Dray was a general practitioner in the New Britain area for many years. He was on the staff of the New Britain General Hospital, and the New Britain Memorial Hospital. Dr. Dray was a member of the American Medical Association and the Connecticut State Medical Society. Dr. Dray died March 10 at the age of 84.

Lonsdale, Henry G., California, Berlin 1922. Dr. Lonsdale formerly practiced neurology and psychiatry in the Hartford area. He was a member of the American Psychiatry Association, the American Academy of Neurology, the American Medical Association and the Connecticut State Medical Society. Dr. Lonsdale died April 2 at the age of 74.

O'Connell, William M., Hartford, Yale 1917. He was a General Practitioner. Dr. O'Connell formerly served on the staff of the Yale-New Haven Hospital, and St. Raphael's Hospital. He was a member of the American Medical Association and the Connecticut State Medical Society. Dr. O'Connell died April 27 at the age of 77.

Prout, Edgar B., Syracuse University 1914. Dr. Prout was a general practitioner in the Hartford area for 20 years. He was a chief physician to the Office of Civil Defense and director of the state blood program for American Red Cross. He was industrial physician and flight surgeon at the Pratt and Whitney Division of United Aircraft Corp. during World War II. He was in general practice in New York City and clinical physician for the New York City Department of Health. Dr. Prout was a member of the American Medical Association and the Connecticut State Medical Society. Dr. Prout died April 21 at the age of 79.

Szlemko, Emile A., Gales Ferry, Geneva 1937. Dr. Szlemko was a general practitioner in Gales Ferry area for many years. He was on the staff of the Lawrence Memorial Hospital. Dr. Szlemko was a member of the American Medical Association and the Connecticut State Medical Society. He served in the U.S. Army from 1943-46. Dr. Szlemko died February 12 at the age of 58.

Tileston, Wilder, Harvard 1899. Dr. Tileston was an internist in the New Haven area for many years. He practiced in Boston for nine years before com-

ing to Yale where he became an assistant professor in medicine in 1909. He became a full professor in 1920. Dr. Tileston was a visiting physician at Yale-New Haven Hospital and a consulting physician at Meriden Hospital and Griffin Hospital, Derby. Dr. Tileston was a member of the American Medical Association and the Connecticut State Medical Society. Dr. Tileston died May 5 at the age of 94.

Science News

To Redress An Imbalance

Human Ecology is becoming a more urgent problem for many scientists as a result of soul searching analysis by them of their present activities. A fascinating and meaningful presentation at March 4th "research" stoppage was delivered by Professor Ronald F. Probst of MIT laboratory of Fluid mechanics. Three years before, he and his colleagues decided to reconvert themselves from working for the military and space-oriented research to become active on socially oriented research. It was not to sever relations with war supported research so much as an effort "to redress an imbalance."

They decided to work in air pollution, water pollution, biomedical fluid mechanics and desalination of water. Even though the problems they undertook "would appear to be vastly different from the type of problems encountered in nuclear explosions or missile re-entry," they were not that different. They all involve fluid mechanical and chemical kinetic concepts. Their real efforts were "in reconverting our own thinking from one area of research to another, but not necessarily in starting from scratch.

The lessons of their courageous imaginative move at MIT are clear: there is a tremendous versatility in the scientific/engineering community that can easily be tapped for much needed research on society's more bedeviling problems. Those scientists and engineers who would prefer this type of research to military research can expect help in reconverting if they take the initiative in seeking research support. Finally both government and industry must recognize the urgency of our societies problems and must be prepared to finance research that might lead to their solution. "Business as usual" is an outworn slogan.—L.H.N. *Scientific Research*, 4: 9, April 28, 1969.

Smoking Interferes With Ability To Utilize Vitamin C

Various investigators have found cigarette smokers more subject to diseases linked to vitamin C deficiency. Pelletus evaluated the vitamin C status in fourteen smokers and fourteen non-smokers and found that smokers excreted about 40 per cent less vitamin C than non-smokers after a saturation and desaturation period. He believed that the marked difference in excretion of vitamin C reflects the amount available for utilization.

The smokers also had lower blood levels of vitamin C. The responsible mechanism may be linked with the absorption of C from the intestinal tract.—L.H.N. *JAMA*, 208: 626, 1969.

Making A Virus Vaccine

The development of a vaccine begins with the discovery of the causal agent, an assessment of its clinical and public health importance and the finding of means for its propagation which are suitable from the standpoint of both safety and economy.

Live virus vaccines must be properly attenuated by still arbitrary means to a point where the reduction in pathogenicity is sufficient to assure clinical acceptability yet not great enough to result in inadequate immunity.

Killed virus vaccines must be properly purified, concentrated, quantified and rendered inactive by procedures which permit retention of antigenicity. Following extensive tests for safety and potency in animals and in cell cultures cautious testing of the vaccine in informed consenting persons is begun, particular attention being given to the benefits the recipient may derive from the vaccine.

Efficacy is measured in terms of the vaccines ability to evoke a significant antibody response and to protect against infection and disease caused by the corresponding virus under conditions of natural exposure for a considerable period after vaccination. Finally with these hurdles passed, the stage of routine manufacture is reached in which it must be demonstrated in the laboratory assay and in tests in man that the vaccine of comparable quality can be consistently produced in serial lots.—L.H.N. Hilleman, M. R., *Science*, 164: 506, May 2, 1969.

AROUND THE STATE

**New Haven County
Board of Governors
April 24, 1969**

New Haven County Medical Association

The new Board of Governors of the New Haven County Medical Association held its first meeting at the Colonial House, in Hamden, on Thursday, April 24, 1969. President Kurt Pelz was named Chairman of the Board, and then appointed the standing and several ad hoc committees.

An Ad Hoc Committee to study the expanding function of the County Review Committee was named. Expansion of the County office space at 362 Whitney Ave., New Haven was voted and funded.

Note was made of the Testimonial Dinner Dance in honor of A. J. Mendillo, M.D. on May 24, 1969 at the Yale Commons.

Donald P. Roach, M.D., of Shelton was elected as a Delegate to fill a vacancy on the Board.

New Haven County Medical Association Delegates to the other counties of the Connecticut State Medical Society were named as follows:

- Bernard A. Burnham, Waterbury to Fairfield
- John J. Mendillo, New Haven, to Hartford
- Jerome K. Freedman, New Haven, to New London
- John H. Flynn, New Haven, to Middlesex
- Elliott Mayo, Waterbury, to Litchfield

Delegates to Tolland and Windham Counties will be named later.

Our Councilor, Dr. Stewart J. Petrie, made an 8 part report in detail bringing the members of the Board up to date on recent actions of the Council of the Conn. State Medical Society.

Forthcoming bills in the State Legislature were reviewed.

Dr. Stewart J. Petrie announced that the Dr. Freiheit Memorial Award sponsored by the New Haven County will be awarded at the Physician Art Association showing at the Annual Meeting of the State Society in Hartford May 13-15, 1969.

The following Resolution was adopted by vote of the Board:

WHEREAS—Charles C. Verstandig, M.D., in his speech as retiring President of the New Haven County Medical Association at its annual meeting March 27, 1969 at the Waverly Inn, made

certain unfounded statements which are very damaging to the reputation and public image of the physicians of New Haven County, AND

WHEREAS—The records of the Review Committee and the Board of Censors of the Association reveal that the physicians of New Haven County, with very few exceptions, have been most circumspect and reasonable in their professional charges to their patients, AND

WHEREAS—Dr. Verstandig, as President of the Association, was present at all meetings of the Review Committee and the Board of Censors of the Association and thereby had personal knowledge that there were very few instances of unjustified charges, and knowledge that these instances were vigorously corrected by the action of these committees

THEREFORE, BE IT RESOLVED, that the Board of Governors of the New Haven County Medical Association does not accept, and indeed regrets, the statements made by Dr. Verstandig.

The next meeting of the Board of Governors is scheduled for Thursday, June 5, 1969 at the Colonial House in Hamden.

The semi-annual meeting of the New Haven County Medical Association is scheduled for Thursday, October 23, 1969 at the Waverly Inn, Cheshire.

The annual meeting of the New Haven County Medical Association is scheduled for Thursday, March 19, 1970, at the Waverly Inn.

Respectfully submitted,
William L. West, M.D., clerk

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Electrocardiogram of the Month

Montefiore Hospital and Medical Center
The Bronx, New York

Editors

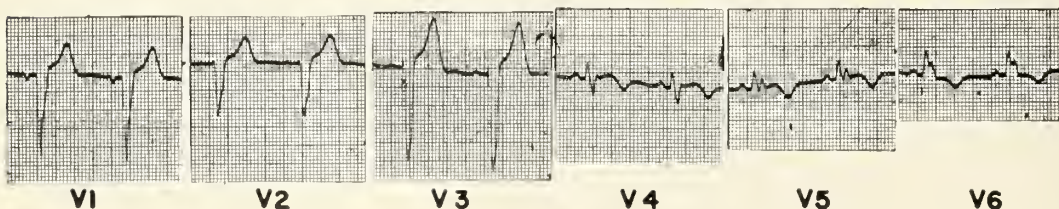
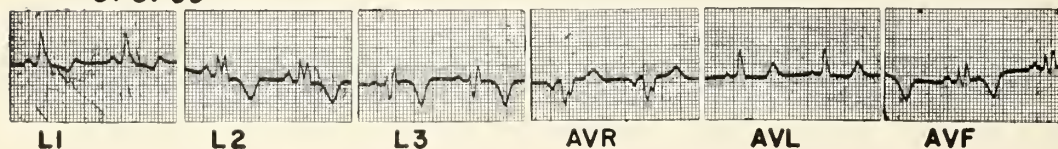
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Head, Department of Electrocardiography

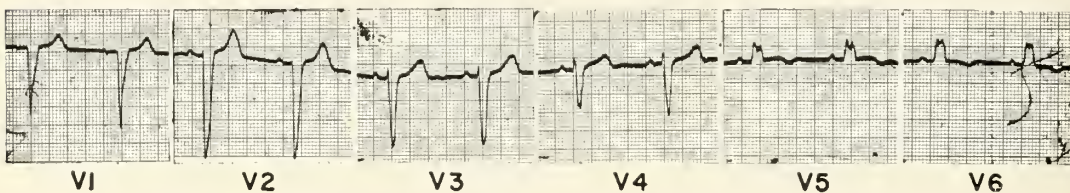
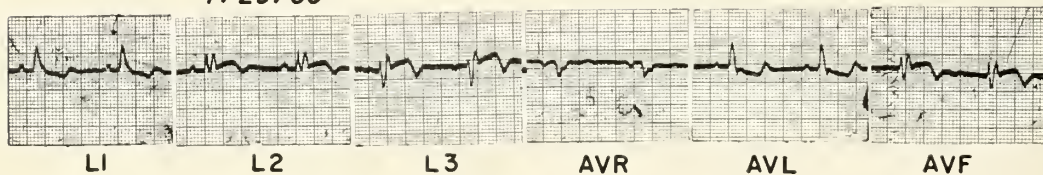
JULIAN FRIEDEN, M.D.

Associate Head, Department of Electrocardiography

8/8/60

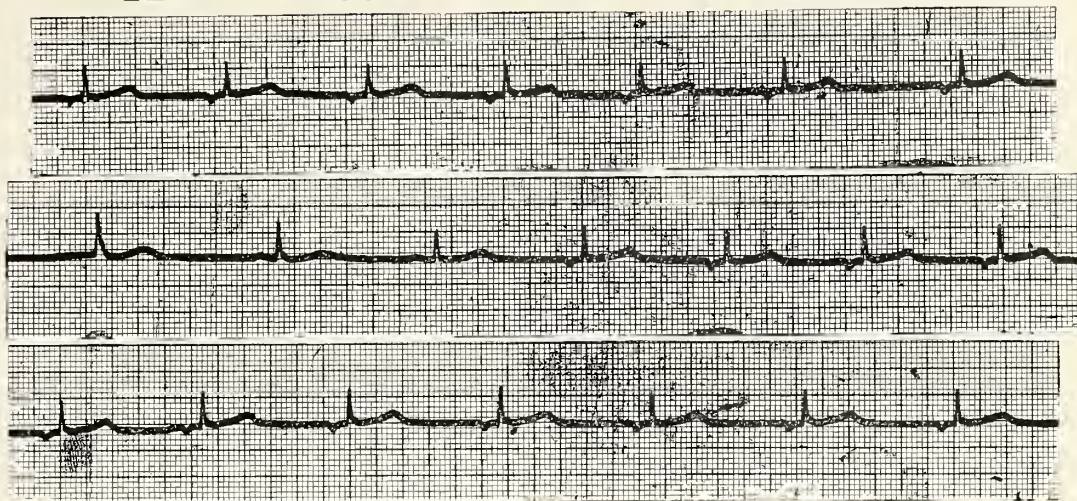


7/29/60



QUESTION 9. What is the diagnosis based on the serial electrocardiograms?

LEAD 2 CONTINUOUS TRACING



QUESTION 10. What is the rhythm?

Electro-
cardiograms
of Month

ELUCIDATION

Question 9. The electrocardiogram dated 7/29/60 shows a QRS duration of 0.14 second. There is no Q wave in leads I, aVl, leads V₄ to V₆; the R wave is slurred and notched in leads V₅ and V₆. These findings are characteristic of left bundle branch block. Of interest is the upwardly bowed, elevated S-T segments in leads II, III, aVf, and V₅. This S-T elevation is unusual in left bundle branch block and could indicate acute myocardial infarction. This diagnosis is further suggested by the deep symmetrical T-wave inversions seen on 8/8/60 in leads II, III, aVf, V₅ and V₆. The T wave is now peaked in V₃. The clinical findings confirmed the diagnosis of acute myocardial infarction. Usually when left bundle branch block is present, the electrocardiographic changes of infarction are masked. In this patient, the electrocardiographic changes confirmed the clinical diagnosis of infarct,

despite the presence of left bundle branch block pattern.

Question 10. In the top strip the P waves are inverted. The P-R interval is 0.15 second. In the second strip the first QRS complex is not preceded by a P wave and is somewhat aberrant in configuration. The next two beats are preceded by upright P waves; the inverted P waves then return.

The diagnosis is coronary sinus rhythm with pacemaker shifting transiently to sinus node. The first beat in strip 2 is of A.V. junctional origin with a P wave buried in the QRS causing the QRS to appear aberrant. Sinus bradycardia then supervenes for two beats, and the coronary sinus mechanism returns at a slightly more rapid rate. This type of rhythm may be seen in the absence of heart disease. This was an electrocardiogram of a sixteen-year-old boy with an innocent murmur.

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Connecticut Medicine

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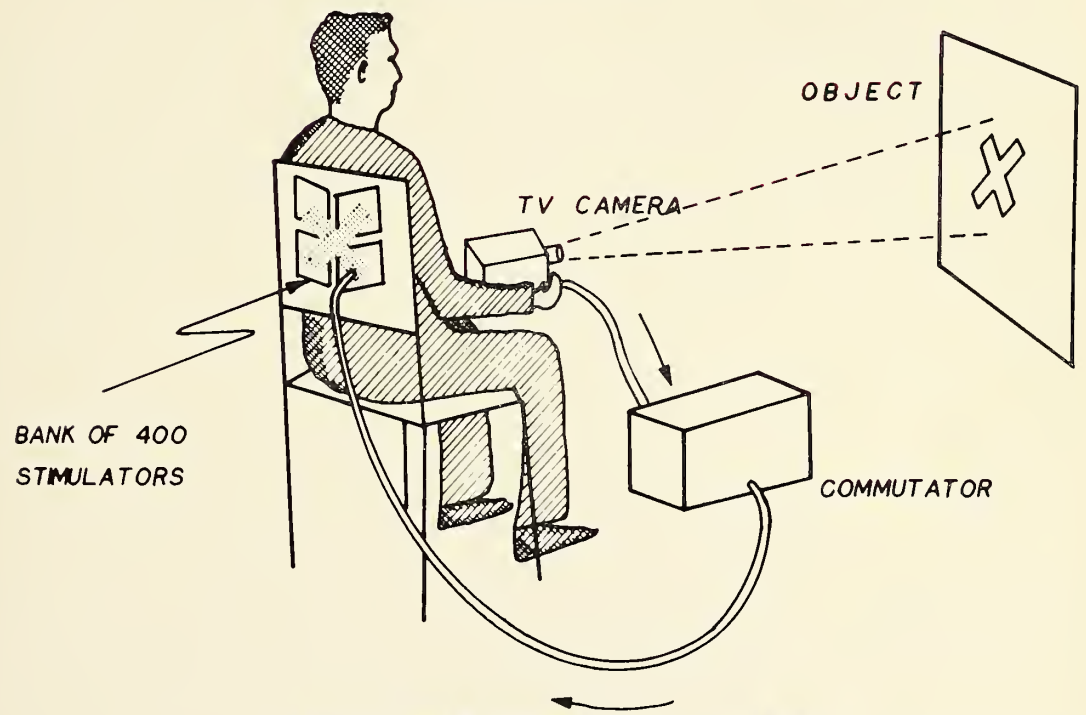
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Connecticut Medicine

Connecticut State
Medical Journal

Volume 33/July 1969/Number 7



TACTILE TELEVISION—see page 425

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Connecticut Medicine

editorials

Science Tools: 33. Tactile Television: A Vision Substitution System For The Blind

*He from thick films shall purge the visual ray
and on the sightless eyeball pour the day.*

—Alexander Pope in the Messiah

A vision substitution system also called tactile television uses the same principle as the children who for generations have played at tracing letters on each other's back. The brain is capable of translating a pattern of stimulated touch receptors into letters and simple images. The same kind of translation of images can also occur when the stimuli come from arrays of electrodes or vibrating points connected to a camera. After a few hours of training blind subjects learn to recognize geometric figures like chairs and telephones.

The skin is the only organ besides the retina that has receptors laid out in a pattern. Dr. Frank A. Saunders declared at the 1969 Neuroelectric Conference. He was stimulated to work on a way to provide the blind with some visual acuity and depth information. It is in their view more important than color or binocular vision. The first experiments on tactile television were begun in 1963 with 3 x 3 and 20 x 20 arrays of vibrating stimulators. The results with 3 x 3 arrays of electrodes used since last summer were identical only the electrical image appears larger and clearer.

They are now developing 20 x 20 array of electrodes mounted in an elastic matrix that can be worn under regular clothes. In their paper, Dr. Saunders and Collins said that the whole system including batteries for eight hours operation may weigh less than five pounds. The system would use a small camera mounted on a blind persons forehead like a miner's lamp. So far most of the data comes from experiments with vibrating stimulators mounted on the back of the subjects chair.

Some blind subjects could recognize real objects after only about an hours training. Even persons who were born blind learned how to judge distance and the relative position of objects through apparent size and overlapping. After about fifteen hours subjects reported that the stimuli seemed to come from in front of the camera—not from the vibrators. "With enough experience the vision substitution system seems to become an automatic extension of the sensory apparatus."

The stimulators were placed 12 mm. apart in both the vibration and electrical experiments. Subjects said that each felt about the same, a sort of buzzing vibration, not unpleasant or painful—like a pinch or pinprick only when the current level was too high. Adequate stimuli were obtained with the current level as low as 50 microwatts. Peak pulse amplitudes between 5-10 milliamperes were described by subjects as "adequate and comfortable" as long as the pulse width range was 10 microseconds or less. Experiments with the electrode ar-

THE COVER

Apparatus developed at the Smith-Kettlewell Institute of Visual Sciences has demonstrated that congenitally blind subjects are able to learn to process visual information when it is presented tactilely. The subject sits in a chair and rests his back against a vibratory matrix. The image received by the camera is translated into impulses which activate the vibro-tactors in a field pattern corresponding to the visual image.

With the apparatus, blind subjects have learned to identify a variety of objects, photographs, letters and words, and to make correct judgments of relative distance and position of objects placed together in complex arrangements.

The immediate goal of this research is the development of a high-resolution system which will provide pictorial and printed information not now readily available to the blind.

ray placed on various parts of the body showed that abdominal skin "sees" better than the skin of the back and forearms.

And so we see the Alexander Pope's vision has come true. Blind persons may soon be able to see with their skins using a tiny television camera point to point image converter and a grid of electrodes worn under their clothes. (see front cover)

L.H.N.

Reference

1. System may let blind "see with their skins." JAMA, 207: 2204, March 24, 1969.

Obesity And Hypertension

The control of obesity and hypertension is an essential part of any coronary heart disease (CHD) prevention program. Both are common major health hazards. They both predispose to CHD. It is also likely that one of the detrimental aspects of obesity is mediated at least in part by the association between blood pressure and weight levels. It may also be that because of their frequent coexistence that these two common conditions have a causal relation between them. If so then weight gain constitutes one kind of environmental stress that brings a genetic predisposition to hypertension into the open. A parallel situation exists in the case of diabetes which may sometimes be controlled by weight reduction, implying that conversely overeating can precipitate it.

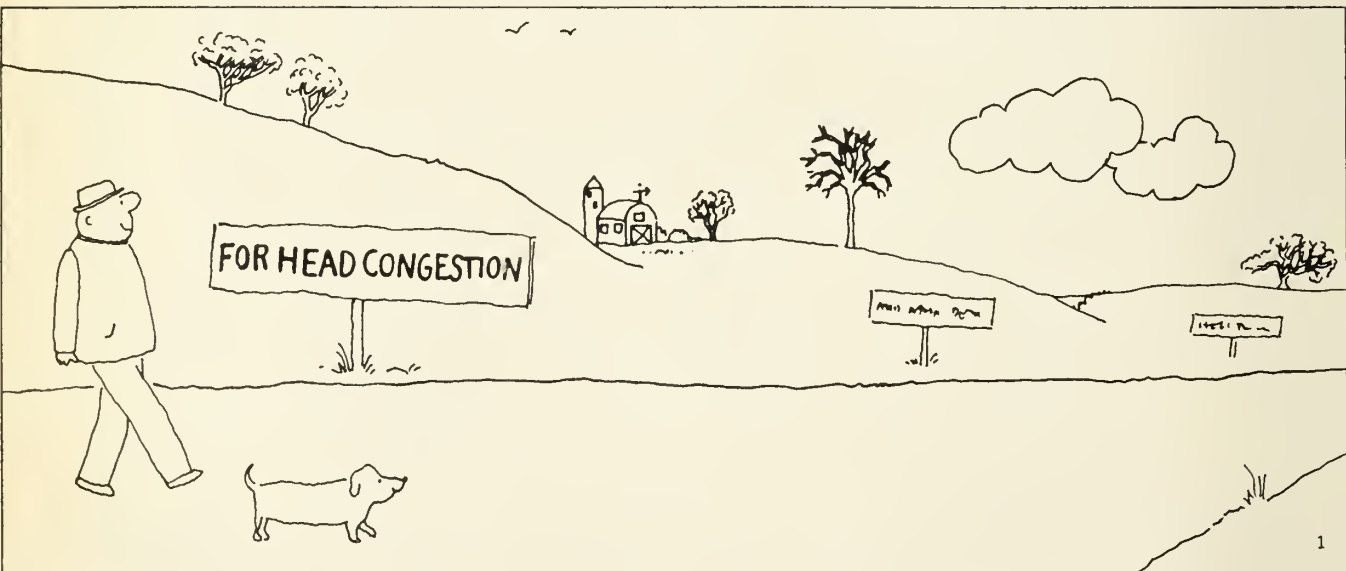
To prevent CHD there must be a constant search for environmental factors that may be modified to delay the onset and progression of atherosclerosis

and its consequences. Weight control is likely to be an important ingredient of any program for the control of hypertension in the community and the individual patient. In this country 30 per cent of men and 40 per cent of women over age thirty are at least 20 per cent above the desirable weight.¹ An individual, of course, may be overweight on account of musculature or bony structure. This means that the component of overweight that can be reduced is fat and every physician must make a clinical judgment of this component.

Prevalence of hypertension 27 per cent of men and 37 per cent of women depends on accepting a dividing line of 160/95 between normal and abnormal. And so we are left with three questions, what is the overall correlation between blood pressure and body weight? What is the proportion of hypertensive persons who are also overweight? Is the correlation between blood pressure and body weight a methodological artefact? The evidence marshalled by Chang et al² is overwhelmingly in favor of the view that body weight and blood pressure are positively correlated.

One may estimate that at least 20-33 per cent of all hypertensive subjects in the adult population are overweight. Such persons have an increased mortality from cardiovascular and cerebrovascular disease. This fact has preventive implications if we work to lower blood pressure and reduce overweight. The measurement of blood pressure by the indirect method have been questioned because of variation in arm circumference and skill in applying the cuff. The method has been compared with intra-arterial measurements and if the cuff is cor-

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rectly applied, then variation in arm circumference is a minor factor in correctly estimating arterial pressure.

The risk of developing hypertension through overweight is clearly portrayed in Chang's review of this subject. The evidence is well marshalled and shows that with few exceptions increase of relative weight over time, is associated with a rise of blood pressure. In various population studies obese hypertensive patients experience a greater risk of CHD and cerebrovascular disease and mortality from these, than do persons with either obesity or hypertension alone.

Furthermore, the risk of subsequent development of sustained hypertension in young adults with obesity or those becoming obese in the ensuing decades is greater than among young adults with normal or less than normal weight who remain lean.

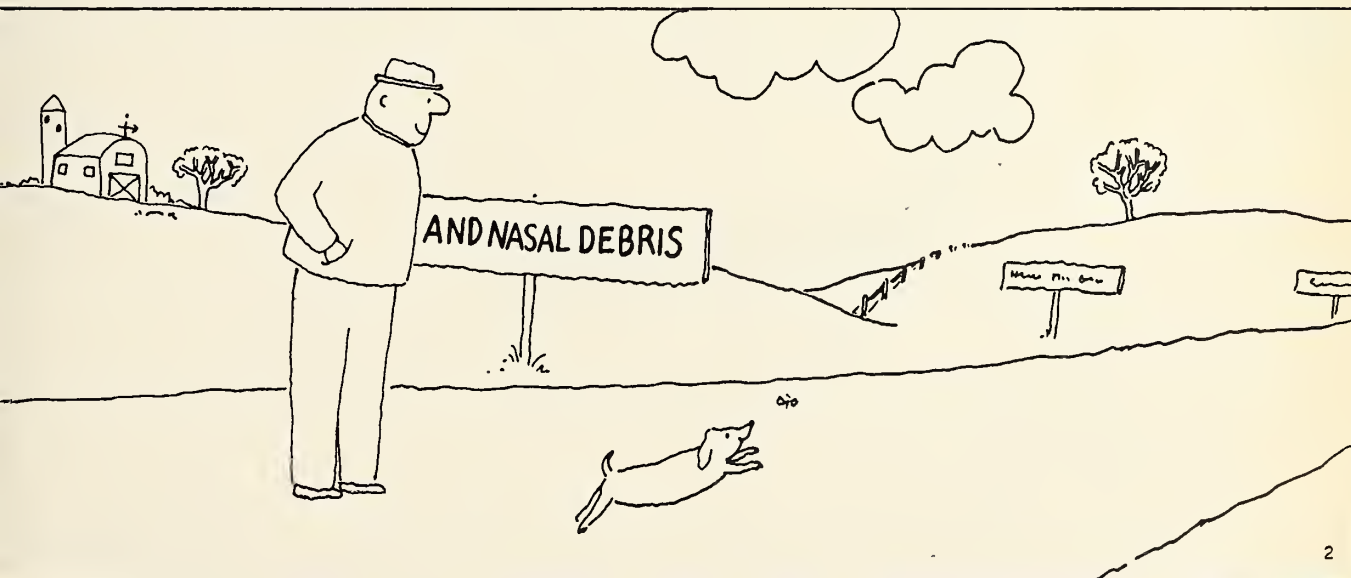
It is difficult to keep patients on a diet and the effect of weight reduction on blood pressure also varies in a considerable portion of obese hypertensive patients. In obesity there is increased blood volume and cardiac output. When this is imposed on patients with hypertension, it may further strain the circulatory system and compromise its functional integrity. Accordingly if the obese hypertensive reduces his weight, it will remove the extra metabolic and hemodynamic burdens that obesity imposes upon hypertension. Thus it seems plausible that weight reduction would diminish circulatory strain and serve to prevent accelerated decompensation in hypertensive heart disease among the obese. This

would be especially valuable when coupled with appropriate anti-hypertensive therapy.

The Build and Blood Pressure Study in 1959³ showed the existence of excessive mortality in overweight persons among all age and blood pressure groups. This excessive mortality is greatest in the younger age groups due primarily to CHD. Conversely there was found an excess of CHD and cerebrovascular disease especially among men⁴ in overweight and hypertensive persons. This has been widely documented in many clinics throughout the land. To be sure some reports differ somewhat because clinical studies in general are likely to be highly selective. The differences, however, that have crept into the literature may be due to the level in the cut-off point in blood pressures considered to be normal.

It still remains difficult to extrapolate these findings to what might be the effect of weight reduction in the population at large. There remains a great need for further documenting the potential benefits of weight loss among obese and obese hypertensive subjects by means of continuing study. However, the converging evidence from a large variety of sources summarized in this review² strongly suggests that the impact of weight reduction in the general population would be very considerable and lessen the burden of mortality as well as morbidity from cardiovascular disease. The inevitable conclusion must be that the control of obesity should be an intrinsic part of any therapeutic or preventive anti-hypertensive regimen.

L.H.N.



References

1. Metropolitan Life Insurance Company, New York. Frequency of overweight and underweight. Stat. Bull., 41: 4, 1960.
2. Chang, B. N., Perlman, L. W. and Epstein, F. H.: Overweight and hypertension: A review. Circulation, 39: 403, March 1969.
3. Build and blood pressure study 1959. Society of Actuaries, Chicago. Vol's. 1 and 2, 1959.
4. Kannel, W. B., Dawber, T. R. and McNamara, P. W.: Vascular disease of the brain: Epidemiologic aspects. Farmingham study. Am. J. Public Health, 55: 1355, 1965.

Systemic Lupus Erythematosus (SLE): A Model For Studying Auto-Immune Diseases

Originally when SLE was described, it was rare, had a poor prognosis and there was a paucity of anatomic causes of death at post-mortem examination. Two developments since then have greatly helped to clarify the clinical picture and also improve the prognosis. One was the observation of the L.E. cell phenomenon by Hargraves et al.¹ The other was the availability of corticosteroid therapy. As a result, the acute febrile manifestations now respond promptly to corticosteroids and the patients survive long enough to develop chronic par-enteral insufficiency especially of the kidney.

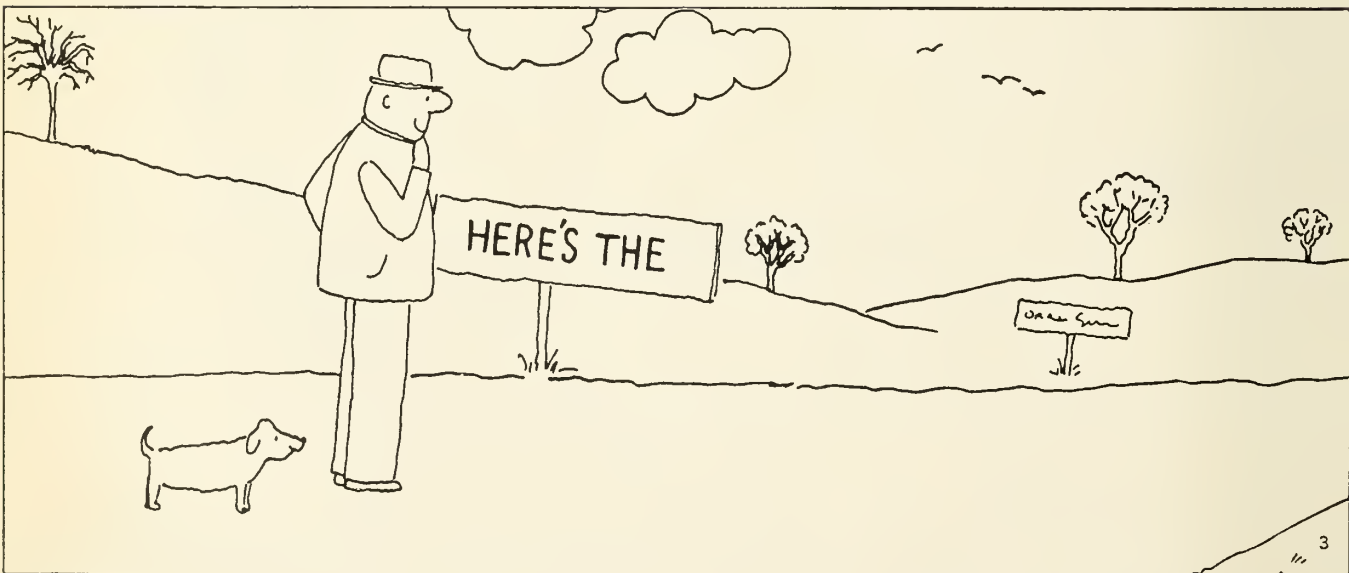
The syndrome typically involves multiple systems, arthritis, serositis, nephritis, dermatitis, and blood cytopenias are common. Neurovascular complications are relatively infrequent but contribute significantly to morbidity and mortality. In this category are stroke, myelitis and peripheral neuro-

pathy. The diffuse vasculitis present also produce ischemic changes in the skin causing ulcers and digital gangrene. There is a rare case that complicate SLE in the form of verrucous endocarditis which, however, rarely causes valvular dysfunction.

The most common cause of death from SLE is now nephritis. It is exactly this same type of nephritis that can be produced experimentally when animals are treated with chronic injections of heterologous serum protein of humans. Because of this similarity we are in possession of an experimental animal model for studying variables which affect the pathogenesis of SLE nephritis. We now recognize two classes of analogous substances that have been implicated as potential sources of antigens for complexes in LSE, nuclear material and gammaglobulin.

By using appropriate techniques of fluorescein labelled antibody, Christian and his co-workers² and Seegal et al³ found granular deposits in SLE glomeruli. Such observations provide strong although indirect support for the pathogenic potential of immune complexes in which nuclear materials are the antigens. It is now thought that nuclear antigen complexed with anti-nuclear antibodies have a comparable role in the development of an SLE like disease in New Zealand mice.⁴

Studies of cryoglobulins in SLE serums have indicated the presence of complexes found by host IgG immunoglobulins and antibodies to IgG.⁵ These cryoproteins resemble the ones with other clinical states such as Hansen's disease and infectious mononucleosis. They have been termed "mixed types" which contain some immunoglo-



bulins, one of which possess anti IgG activity. A syndrome of purpura, myalgia and glomerulitis is associated with "mixed type" cryoglobulins. Like SLE, the syndrome has all the marks of an "immune complex" disease. Clearly, complexes formed by the reactants of mixed globulins may be pathogenic.

Thus the recognition that immune complexes formed with autologous antigens may be injurious, has added a new dimension to auto-immunity. In the "immune complex" model autologous antigens regardless of their origin can induce diffuse vascular injury when combined with corresponding auto-antibodies. There is an extensive array of autologous substances that are varyingly reactive with antibodies in SLE subjects, nuclear antigens, ribosomes, IgG globulin, cardiolipin and blood coagulation factors. These and other autologous antigens when complexed with antibodies probably mediate some of the vascular abnormalities of SLE. In addition to autologous antigens in the pathogenesis of SLE there is no reason to rule out the participation of exogenous environmental antigens, such as bacteria, viruses and even some drugs.

Some patients with glomerulitis show diffuse involvements and speedy death. Others show only focal involvement and do not manifest progressive renal failure. Accordingly the basic question is whether the glomerulitis is focal or diffuse. If focal the prognosis is good, if diffuse the prognosis is poor. As far as therapy is concerned, we know that corticosteroid treatment of SLE nephritis in doses of 50 mg. prednisone daily leads to reduction in proteinuria and suppression of anti nuclear antibody. There is a clinical impression that antimeta-

bolite therapy by drugs such as azothioprine and cyclophosphamide can suppress active manifestations of SLE, and that patients who receive such drugs may be managed on smaller doses of corticosteroids. Controlled studies to settle this question are needed but these would involve questions as to whether denying therapy to patients in the control group would be unethical.

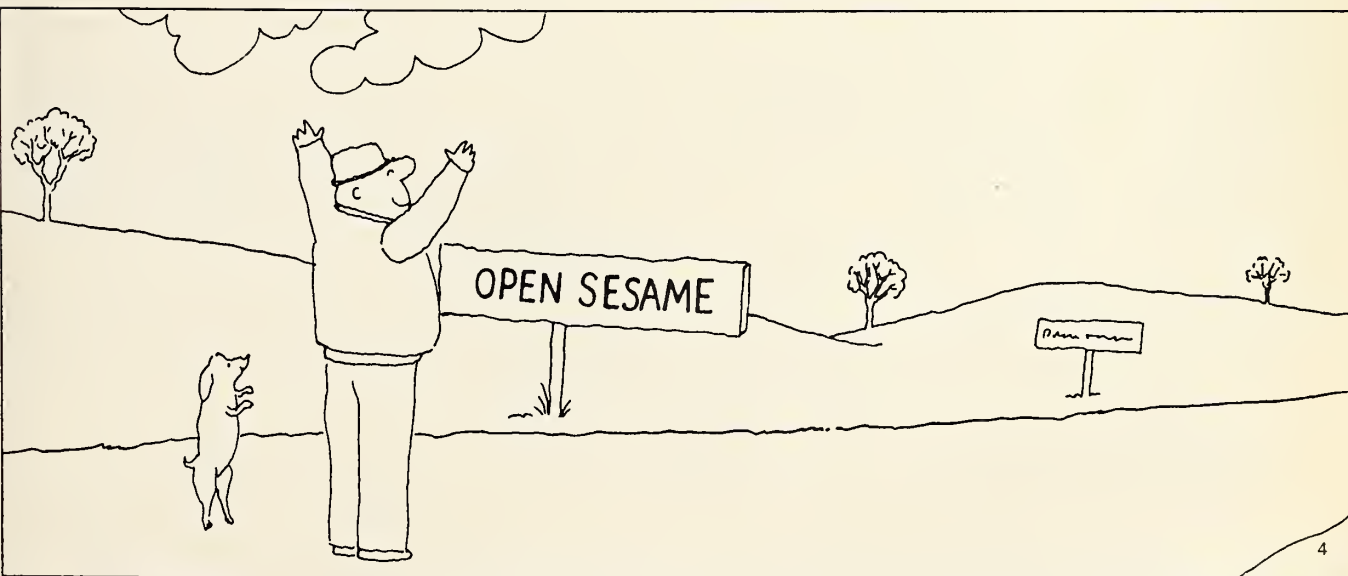
We must not forget that SLE tends to be a spontaneously remitting disease. Unfortunately the kidney unlike some other organs has a limited capacity for repair. This is probably why there are an increasing number of patients who have exhibited typical features of SLE but who now manifest slowly progressive chronic renal disease. It could be that more intensive therapy during the active phases of glomerular injury will lessen the likelihood of irreversible renal damage.

In sum we now know that renal disease in SLE and chronic serum sickness in animals show many features in common and in both it appears to result from glomerular localization of soluble immune complexes. In animals with chronic immunization, we find the production of non-precipitating antibodies forming in vivo relatively of small size, soluble, which circulate for periods of several hours and these animals manifest chronic glomerulitis. Nuclear antigens in association with nuclear antibodies may account for similar circulating immune complexes in SLE in man.

L.H.N.

References

1. Hargraves, M. M., Richmond, H. and Morton, R.: Presentation of two bone marrow elements: "tart" cell and L.E. cell. Proc. Staff Meet, Mayo Clinic, 23: 25, 1948.



2. Christian, C. L.: Immune-complex disease. *New Eng. J. Med.*, 280: 878, April 17, 1969.
3. Seegal, B. C. et al: Immunofluorescent studies of lupus nephritis. *Fed. Proc.*, 27: 544, 1968.
4. Lambert, P. H. and Dixon, F. J.: Pathogenesis of glomerulo nephritis of NZB mice. *J. Exper. Med.*, 127: 507, 1968.
5. Hanauer, L. B. and Christian, C. L.: Studies of cryoproteins in systemic lupus erythematosus. *J. Clin. Investigation*, 46: 400, 1967.

Drug Metabolism And Therapeutics

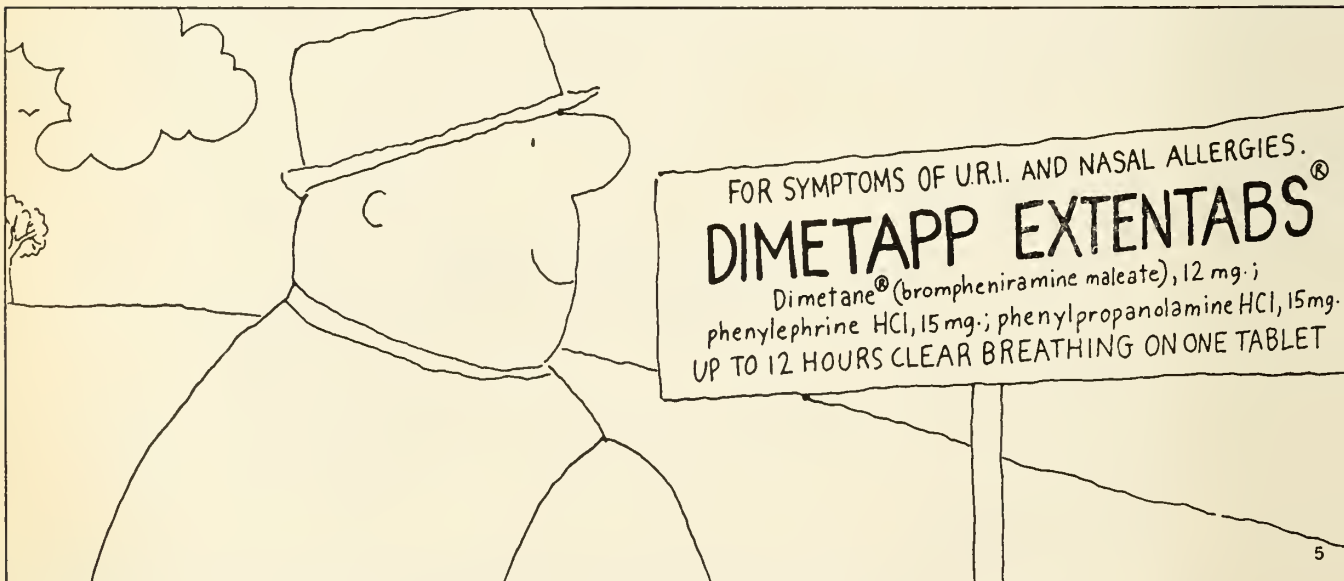
There is widespread administration of multiple medications to a single patient. This demands an increased awareness of both the metabolic effects of drugs and also the possible effects of one drug on the metabolism of another. We now know that the duration and intensity of action of many drugs in animals depends on the activities of drug metabolizing enzymes located primarily in the endoplasmic reticulum of the liver cell. These enzymes catalyze the metabolism of therapeutic agents by many different pathways particularly by hydroxylation and glucuronide formation.¹

Phenylbutazone is converted into two metabolites, one antiinflammatory and the other uricosuric. Imipramine's antidepressant action is due to a metabolite desmethylimipramine. Chlorpromazine is converted to many different metabolic products which differ in different people in their rates of formation and disappearance. It is this which accounts for individual variation of biologic activity. Young growing livers as in neonates and newborns have little ability to cope with drugs and are more sensitive than adults to drugs and so may suffer

neonatal anoxia and even death if drugs are given to the mother. As the livers grow older metabolizing enzymes do appear. Even then some patients will metabolize a drug so rapidly that they cannot achieve an effective therapeutic blood and tissue level, while others metabolize a drug so slowly that toxic effects can result.

Coumarins^{2, 3} are metabolized at widely varying rates from one to more than 10 fold. This is why it is so difficult to predict dosages needed to obtain the desired prothrombin time. Large individual differences are also encountered with imipramine and responses to a given dose may vary as much as 36 times greater than the person with the lowest level. In the person with high levels the side effects can be reduced by phenobarbital which is known to enhance drug metabolism in the liver. Administration of dilantin likewise shows very wide variability in blood levels in different individuals ranging from 2.5 to over 40 mg. per liter following the same dose. Marked individual variations also exist in the metabolism of phenylbutazone, antipyrine, isoniazid, succinylcholine. Genetic factors have been shown to play an important part in explaining individual differences in metabolism of these and many other drugs. In fact individual variability in response to the same dose of a drug is a universal phenomenon.

The idea that one drug can simultaneously stimulate or inhibit the metabolism of another may be the important determinant of individual variation in the metabolism and action of drugs. Fifteen years ago Axelrod, Brodie et al found a drug that could prevent metabolism of hexobarbital. They



explained this by an effect of the drug 525A on liver microsomal enzymes that normally metabolize hexobarbital to inactive products. There are now many examples of inhibition of drug metabolism documented in man: phenylbutazone, sulphaphenazole, dicumarol inhibit inactivation of tolbutamide and can cause profound hypoglycemia. Likewise giving dicumarol and dilantin will result in toxicity because the dicumarol inhibits the metabolism of dilantin.⁴

Drugs that are strongly bound to serum albumin can displace the coumarins and increase anticoagulant action to the point of hemorrhage. Phenylbutazone does this, so do sulfonamides, salicylates and other acidic drugs. Severe hypertensive reactions have occurred when patients treated with a monoamine oxidase inhibitor such as iproniazid, ingested cheese or other foods with a high tyramine content. The reason is that the iproniazid interferes with the enzyme that metabolizes sympathomimetic amines.

Sometimes, however, the opposite occurs: chronic administration of one drug may reduce the pharmacologic activity of another by increasing the amount of drug metabolizing enzymes in the liver leading to inactivation of the drug. This is termed enzyme induction. Drug metabolism can be stimulated by many different types of drugs such as phenobarbital, antihistamines, oral hypoglycemic, and uricosuric agents, and by chemicals found in the environment such as DDT and one powerful enzyme inducer is 3-4 benzpyrene found in cigarette smoke. There have now been described over 200

drugs and other chemicals that stimulate drug metabolism in animals.

Zoxazolamine is a muscle relaxant which can last eleven hours but after pretreatment with phenobarbital, will last but two hours and after pretreatment with 3-4 benzpyrene will last seventeen minutes. The enzyme induction alters the intensity as well as duration of drug action. Thus treatment of animals with enzyme inducers decreases the toxicity of meprobamate, pentobarbital, strychnine, coumarin, phenylbutazone and lidocaine. In man phenobarbital induces liver microsomal enzymes that metabolize coumarins and this reduces anticoagulant activity. Once phenobarbital is discontinued that plasma levels of coumarin rises again and prothrombin time returns to original level. It could be hazardous if phenobarbital is discontinued while the high coumarin level is maintained. Phenobarbital stimulates metabolism of other clinically useful drugs. Dilantin levels become lower in the plasma and its anticonvulsant level may be lost.

Then there is the observation that chronic administration of a drug not only stimulates the metabolism of other drugs but in many cases may lead to enhancement of its own metabolism.⁵ This is why we often encounter growing tolerance when a drug is given chronically. This may be true of the barbiturates and meprobamate. In the case of morphine and meperidine tolerance is not due to increased metabolism but to altered sensitivity of the central nervous system to the drug.

Phenobarbital after several days also increases activity of enzymes in the liver microsomes that

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hydroxylate androgens, estrogens, progestational steroids and glucocorticoids. Several other drugs do the same such as dilantin, chlorcyclizine, phenylbutazone and DDT. The result is decrease in plasma levels as a consequence of acceleration of their metabolism. Furthermore, the enzyme inducers also accelerate metabolism of cortisol. Because phenobarbital leads to glucuronide conjugation of bilirubin in liver microsomes it has been used successfully in two infants with congenital non hemolytic jaundice. Phenobarbital also has been found useful in lowering serum bilirubin concentrations in patients with chronic intrahepatic cholestasis.⁶

In pregnancies in which one might anticipate increased bilirubin formation by the newborn baby the use of phenobarbital may provide a method other than exchange transfusions for reducing the concentration of neonatal bilirubin in infants. We must remember however, that phenobarbital can lead to increased metabolism of steroid hormones and other normal body substrates. And so this treatment must be approached with caution and it is at present not known what harmful effects might result.

We will now think of using enzyme inducers to treat diseases of overproduction of steroids. May it be possible to treat other genetic diseases besides hyperbilirubinemia with specific enzyme induction. We know that phenobarbital causes increase in liver weight, in microsomal protein content, enhances bile flow, increases liver function and stimulates metabolism of a variety of normal body substrates. This raises the obvious question of whether phenobarbital and other enzyme inducers could be used in the treatment of certain forms of liver disease requiring liver regeneration. Finally we need to learn whether the 3-4 benzpyrene in cigarette smoke (which is the most powerful enzyme inducer) alters the metabolism and action of other commonly used drugs.

L.H.N.

References

1. Conney, A. H.: Drug metabolism and therapeutics. *New Eng. J. Med.*, 280: 653, March 20, 1969.
2. Weiner, M. et al: Physiological disposition of dicumarol in man. *J. Pharmacol. and Exper. Therap.*, 99: 409, 1950.
3. O'Reilly, R. A. and Aggeler, P. M.: Coumarin anticoagulant drugs: hereditary resistance in man. *Federation Proc.*, 24: 1266, 1965.
4. Hammer, W., Idestrom, C. M. and Sjoquist, F.: Chemical control of anti-depressant drug therapy. In *International Congress Series No. 122. Proceedings of the First International Symposium on Anti-depressant Drugs*, Milan, 25 April

1966. Edited by S. Garattini and M. N. G. Duker. Amsterdam, Netherlands. *Excerpta Medica*, 1967, pp. 301.

5. Aggeler, P. M., O'Reilly, R. A., Leong, L. and Kowitz, P. E.: Potentiation of anticoagulant effect of coumarins by phenylbutazone. *New Eng. J. Med.*, 276: 496, 1967.

6. Maurer, H. M. et al: Reduction in concentration of total serum bilirubin in offspring of women treated with phenobarbital during pregnancy. *Lancet*, 2: 122, 1968.

Control Of Viral Infections: Immunologic Methods

At present there are only three approaches to the specific control of infections caused by viruses. Immunologic control, host resistance and chemical control. We all know how remarkably effective immunologic control has been in affording protection for the long or relatively long term. There is, however, one disadvantage namely that the spectrum of viral strains against which it gives protection is narrow. Host resistance as exemplified by the interferon mechanism promises broad spectrum antiviral activity. Its disadvantage is that the effect is of short duration. Chemical methods for controlling viral infections have thus far given meager rewards and have two disadvantages. The spectrum of strains against which they give protection is narrow and to maintain a protective effect the chemical substance must be administered continually.

Vaccine against smallpox is now well developed. In the process of development are vaccines against rabies and arboviruses of which Japanese B Encephalitis are examples. This latter is of especial urgency since it is said to be one of the diseases in the arsenal of bacteriological warfare. The vaccine against yellow fever virus which has been attenuated and propagated in chick embryo or in mouse brain, has yielded effective control of this disease.

In the respiratory complex the first one to yield to vaccine approach were influenza A and B also developed from virus grown in chick embryo but then killed with formaldehyde. The irritants formerly present have now been eliminated by ultracentrifugation. The problem, however, is that every ten years or so major changes occur in the A strain with near total antigenic alteration, thus rendering previous immunity non-effective. Even minor changes may occur which markedly reduce the effectiveness of the vaccine necessitating periodic revision of the strain composition of the vaccine. The last pandemic occurred in 1947 and 1957. This contemporary 1968-69 outbreak "Hong-Kong In-

fluenza" has already swept through much of the northern hemisphere and is expected to cause epidemics in the southern hemisphere in mid 1969.

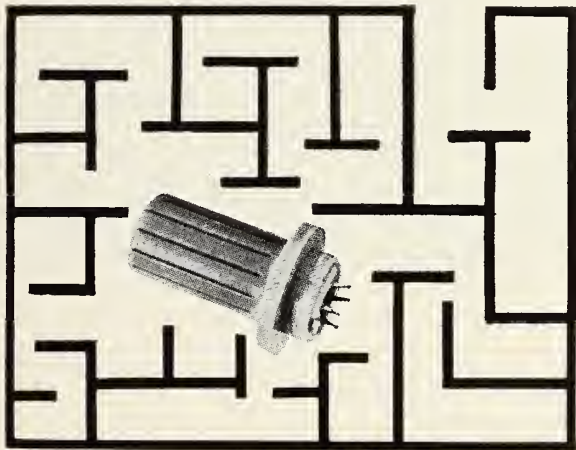
An urgent need is for a vaccine providing protection against a greater number of strains. Also mycoplasma pneumonia, a bacterium has been given attention because of the high incidence of atypical pneumonia. Hilleman and his colleagues¹ have now produced a very efficient vaccine against mycoplasma and it should soon be available for the general population. The rhinoviruses which are a principle cause of the common cold with too many strains offer little hope of a polyvalent vaccine. Immunity to influenza and certain other respiratory viruses appears to depend mainly upon the presence of neutralizing antibody in the respiratory secretions and methods to increase respiratory IgA gammaglobulin should make vaccination more effective.

Among the enteroviruses the most spectacular successes has been with polio. In the case of ECHO and coxsackie viruses which cause considerable amount of respiratory enteric and other illnesses, there is too great diversity in serotypes, making the vaccine approach impossible. Here we must search for ways to achieve induction of host resistance.

There has been no significant progress in specific control of viral hepatitis because the agent has not yet been isolated. Of the Herpes, group, development from live attenuated virus of a vaccine effective against chickenpox and herpes zoster is within sight now that the virus can be propagated in cell culture and such vaccine may be readily available in the next several years. We are almost at the point of elimination of three myxoviruses, measles, mumps and rubella by an attenuated vaccine containing the three viruses. Also adjuvants are being developed which are readily metabolizable and emulsion innoculum which stimulates production of circulatory antibodies at a concentration which is essential for protection of the respiratory tract which may last for more than one season.

It was practicable cell culture technology introduced by Nobel Laureate John Enders which brought new knowledge about viruses, led to development of many vaccines but presented also many new problems. One was the presence of extraneous agents in the vaccines which has now been solved by ultracentrifugation. Another problem was the adverse effect of the virus itself which has not been overcome by techniques of attenuation. A third problem was which cells should be used for preparation of the vaccine. This last was especially challenging because some cells themselves contain viruses as monkey kidney containing SV. 40 virus which produces neoplasia in hamsters. The most recent alarm with respect to extraneous viruses arose over the occurrence in grivet monkeys in Germany of an infection highly communicable to man and caused seven deaths among laboratory workers or people with whom they came in contact. This agent can now be removed and is no longer a threat.

Development of vaccines is also complicated by considerations of whether a given cell will accept the virus for propagation. At present the USPHS regulation permits only primary cell cultures for animal tissues to be used for propagating viruses for preparing vaccines. Cultures from propagated or serial passage are not allowed. This, however, is criticized by some students of virology on the ground that viruses can be oncogenic and would not like to see administration to man of any oncogenic viral genetic material or neoplastic host genetic material carried by a virus. Accordingly they prefer the use of serially propagated cells in which the chances for introduction of a new virus by fresh tissue is excluded.



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On the other hand some regard cancer as a state of the cell itself and prefer that primary cultures be used since they would wish to be sure that the cell was normal with regard to karyosome morphology, propagability and contact inhibition *in vitro*. The argument is not yet resolved. The simple fact is that we do not know the cause of neoplastic disease in man and we do not know whether it is transmissible under any circumstances. We do not know whether any of the factors that have been debated are of any basic importance in the development and transmission of cancer in man. We are waiting for guidelines.

L.H.N.

Studies In Human Ecology: Trace Metal Poisoning And Deficiency In Relation To Health And Disease

In 1900, in Manchester, England, beer was contaminated with arsenic. It involved over 6,000 patients of whom 70 died and nearly all were cardiac deaths.¹ In late 1963 and early 1964 certain brewers both in Canada and this country began adding cobalt to beer in order to stabilize the foam. Within months an epidemic form of fulminating cardiomyopathy recognizably different from alcoholic cardiomyopathy and beri-beri occurred in Quebec City. Later the syndrome was also identified at the Veteran's Hospital in Omaha, Nebraska, Minneapolis, Minnesota and in Leuvan, Belgium.^{2,3}

It is impossible to estimate the total number of cases that occurred around the world but some idea might be gained from the knowledge that about 25 per cent of all the beer sold to metropolitan centers in the United States from 1964-1966 contained cobalt. Beer was also suspect in England, Australia, and Belgium where Kestebol et al found cobalt in half of forty-two brands of beer listed.

The Canadian investigators as a result of "masterful sleuthing recalling Sherlock Holmes" discovered that the victims had consumed large amounts of one brand of beer that subsequently was shown to contain 1.2 ppm. of cobalt. Polycythemia, pericardial effusion and thyroid hyperplasia were seen at autopsy. These unusual features of the syndrome led them to suspect that cobalt might be involved. The serum enzymes were enormously elevated but promptly returned to normal with recovery. There was, however, an alarmingly high mortality in the Quebec and Australia groups, 40-50 per cent

which probably resulted from the severe acidosis and shock encountered in a high proportion of their patients. In contrast only three of sixteen patients in Minneapolis died and none in Belgium died of their acute illness. Probably this difference is due to a dose-response relationship.

Follow-up observations are presented by Sullivan et al² who showed that late cardiac deaths and serious residual cardiac and neurological disability can be expected in some patients. The hearts of autopsied victims contained ten times more cobalt than normal. In consideration of the pathophysiology three conditions seemed basic to its development, alcohol, a protein poor diet acting synergistically with cobalt. In the liver alcohol is oxidized to acetaldehyde and acetic acid and this indirectly may be responsible for impaired fatty acid oxidation, increased synthesis of triglycerides and glycogen depletion of the liver. We do not yet know how the myocardium oxidizes ethanol. But if alcohol impairs fatty acid oxidation, it could seriously impair utilization of this important source of energy by the myocardium. We do know that at least in rabbits alcohol itself does not significantly alter coronary circulation.¹

It is not clear whether this is the explanation of abnormal hemodynamics and contractility in alcoholic heart disease. Thus far myocardial biopsies of the myocardium contained increased glycogen similar to what was found also in cobalt treated rabbits. There is probably also a metabolic disturbance in the production and utilization of glycogen as a source of energy as deduced from mitochondrial changes that are similar in alcoholic and cobalt damaged hearts. Wiberg, Munro and Morrison have shown in rats treated with cobalt that the myocardium is unable to utilize pyruvate and fatty acids for energy. As a result pyruvate proceeds to glycogen and the fatty acids to triglycerides.^{3,4,5}

Decreased cardiac output by a failing myocardium leads to peripheral vasoconstriction as a compensatory mechanism, ischemia, lactic acidosis and in turn this stimulates ventilation. Hypocapnia follows accentuating vasoconstriction, further ischemia and further lactic acid liberation. Obviously the rational basis of therapy should be aimed at breaking this vicious cycle; isoproterenol and digitalis to support the failing heart, bicarbonate to correct the lactic acidosis and perhaps small doses of morphine to slow respiration. As yet no method has been found for removing the excess cobalt from the tissues.



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Warnings: Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia.

In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.

Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.

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The third factor, protein depletion, is well documented by experimental evidence. When cobalt is given parenterally it is much more toxic than when given orally. Cobalt chelates with glutathione, cysteine and histidine derived from proteins, so that by giving protein or these amino acids in the diet, these materials can prevent chelation with sulph hydryl groups in the tissues. The beer drinkers who developed the syndrome invariably were suffering from anorexia and inadequate food intakes whereas others drinking equal amounts of the same beer but eating normally remained well.² This also explains why anemic individuals treated with 100 to 150 mg. of cobalt chloride daily for many months, but ate well, rarely suffered injury to the heart.

Cobalt cardiomyopathy is thus the second known metal induced disease by contaminated beer. Such experiences should stimulate investigation of trace metal poisoning as well as deficiency in relation to health and disease. There have not been any new cases of this syndrome since cobalt was removed from beer and this substantiates the unique association of the described cases with this metal. We now are about to have a new agency CEPHS that will be concerned with environmental factors in health and disease that should have jurisdiction over what industry does with products that man consumes.

L.H.N.

References

1. Bayaner, H. G.: Influence of alcohol on coronary function in rabbits with atherosclerosis induced by cholesterol. *Nature*, 221: 1066, March 15, 1969. (This investigation shows that chronic oral ingestion of alcohol does not significantly alter coronary function. It also confirms the finding that such treatment does not prevent, accelerate or accentuate the development of coronary atherosclerosis.)
2. Sullivan, J. F., George, R., Bluvus, R. and Egan, J. D.: Myocardiopathy of beer drinkers. *Ann. Intern. Med.*, 70: 277, February 1969.
3. Alexander, C. S.: Cobalt and the heart. *Ann. Intern. Med.*, 70: 411, February 1969.
4. Holly, R. G.: Studies in iron and cobalt metabolism. *JAMA*, 158: 1349, 1955.
5. Wiberg, G. S., Munro, I. C. and Morrison, A. B.: Effect of cobalt ions on myocardial metabolism. *Canad. J. Biochem.*, 45: 1219, 1967.

Studies In Human Ecology: Power Station Pollution

Fears of creeping contamination of the environment by waste products from nuclear power stations are widespread, and are bound to grow as more and more such power stations are built. The Interna-

tional Atomic Energy Agency has just published a handbook on the performance of the waste management facilities. It claims that such fears have "thus far" been unfounded. In fact it claims that thus far the disposal of waste has been "excellent." In no case has there occurred any exposure in the plant environs. It should be possible given some care in future plant design to maintain the good record. The report, however, does not envisage any radical change in waste management apart from the relatively minor engineering modifications of existing systems and it unfortunately does not attempt to guess how wastes from breeder reactors can be managed. These will surely present new problems like learning how to deal with contaminated liquid metal coolants.

Apart from these soothing conclusions the IAEA report publishes four reviews of waste management in Canada, France, Britain and the United States. These echo the general air of cheerful confidence although the U.S. Report written by Dr. Morton I. Goldman does point to two areas which may pose problems in the future, the release of tritium from light water cooled reactors and the possible contamination of the secondary water in pressured water reactors by leaking steam generator tubes.

The difficulty with tritium which is a long half-life nucleide is that it is hard to separate from other waste materials. But it is only likely to be a problem on "dry" sites where the cooling water is recirculated through cooling towers. In these circumstances Dr. Goldman says it is conceivable that the tritium concentration could reach unacceptable levels. Finally he says the steam generator leaks have occurred in most if not all operating PWR's releasing contaminants into the secondary water which is supposed to be perfectly clean. This could impose a shutdown of the station "because of an otherwise relatively minor leak" unless there were facilities for decontaminating secondary water. Such facilities will therefore have to be included in future designs.

Meanwhile two American engineers have published an equally anodyne report on the subject of so-called "thermal pollution" in thermal or nuclear stations. Wesley O. Piper, Professor of Civil Engineering at Northwestern University and L. P. Beer previously a senior staff engineer at Consolidated Edison writing in *Electrical World* say that concern about thermal pollution has been exaggerated. They arrived at this conclusion from a study of thermal power stations at Waukegan, Illinois which has been discharging 760,000 gallons

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of warm water into Lake Michigan every minute for the last forty years. Conn Ed. now hopes to build a nuclear power plant at Zion seven miles beyond Waukegan which would treble the amount of warm water being pumped into this part of the lake which is probably why the survey was undertaken.

The water from the thermal plant was at 57° F., 11° F. above the ambient. However, Piper and Beer could find no evidence of environmental damage. No temperature differential could be detected 3,000 feet from shore and the hot water had not affected the water chemistry in any significant degree. Bottom living organisms vital in the food chain of fish had not been eliminated and trout and salmon even near the outlet had suffered no "apparent" shock. Professor Piper claimed that the combined heat input from the two power stations would raise the average water temperature by less than 0.1° F. during one summer. "This increase" he added rather surprisingly would be nullified during the following winter.

The Lake Michigan survey produced results similar to those reached by the Tennessee Valley Authority which undertook surveys in lakes and rivers near TVA power stations. "Personally I am much more alarmed over organic pollution from sewage and from oil pollution" added Professor Piper. "Oil pumped into Lake Michigan with the bilge from lake boats does a great deal more damage to lake life than any possible thermal damage." With this even the most ardent conservationists agree.

What was not considered were the synergistic effects of these two pollutants which may be more serious than either one alone. This is a task that should be undertaken by the new Consumer Protections Citizens, Environmental Service of the Department of Health, Education and Welfare.

L.H.N.

References

1. Power Station Pollution. *Nature*, 221: 894, March 8, 1969.
2. Management of radioactive wastes at nuclear power plants. IAEA. (2. 10s)
3. Piper, W. O. and Beer, L. P.: Thermal pollution. *Electrical World*, February 10, 1969.

Cardiomyopathy From Sympathetic Storms In Cerebral Hemorrhage

Negative T waves in the electrocardiogram are seen frequently in association with acute cerebral hemorrhage and infarction. Such changes suggest the development of ischemic cardiomyopathy.^{1,2}

Burch and his colleagues in fact did find lesions in the myocardium by histochemical techniques in some mice in whom intracranial hemorrhage had been induced experimentally. Ultra structural myocardial changes also occur in mice after simulated intracranial hemorrhage. The lesions were focal and the mitochondria showed various states of degeneration. The sarcoplasmic reticulum was markedly dilated. The myofibrils in some specimens demonstrated a conspicuous lack of striations. The actin and myosin filaments were reduced in thickness and tended to blend together giving the appearance of focal dissolution of sarcomere segments. The chromatin granules of nuclei in the damaged myofibrils were usually distributed along the nuclear membrane.^{3,4} Evidently there were "sympathetic storms" during cerebral injury in mice.

Acute myocardial lesions are seen in virtually all autopsies following cardiovascular surgery as well as in patients who died following subarachnoid hemorrhage.⁵ These may have contributed to the poor cardiac function seen in some patients following cardiac surgery. Investigators at the University of Washington School of Medicine have now induced what appears to be the same type of lesion in rats and cats which are morphologically similar to the human lesions. In the rat a single 50 mg./kg. subcutaneous dose of isoproterenol induced both reversible and irreversible changes in the myocardial cells. The same thing was caused by applying electrical stimuli to the midbrain reticular formation even in the absence of the adrenals.

This raises the possibility that the myocardial injury results from excessive local release of catecholamines presumably the norepinephrine from the cardiac sympathetic nerve endings. Under the electron microscope Reichenbach⁵ reported that nerve endings in the heart of the stimulated animals appear swollen and have decreased number of vesicles as well as granular-vesicles. This could be explained by release of neurotransmitter substances. In both isoproterenol stimulated rats and electrically stimulated cats, the heart lesions healed with interstitial fibrosis.

The lesions both in animals and humans are accompanied by only a little inflammation and primarily injures the muscle cell sparing other tissue components. The lesions appear within ten minutes of stimulation and affect most frequently the cells beneath the ventricular endocardium. As in Burch's mice the most characteristic features are transverse bands with intervening granularity.

The experimental lesions can be augmented by several means Dr. Reichenbach stated, including alterations of sodium and potassium levels, non-specific stress and administration of steroids. This makes it likely that with these other factors involved a stimulus far less drastic than midbrain stimulation could also cause the myocardopathy.

We now have the explanation as to why some patients with cerebral hemorrhage or infarction develop characteristic electrocardiograms of cardiomyopathy. Furthermore, the experiments provide some support for the speculation of others of the role of emotional and psychological stress in inducing catecholamine release and subsequent cardiac injury. There can indeed occur sympathetic storms from cerebral injury.

L.H.N.

References

1. Burch, G. E. et al: Effects of experimental intracranial hemorrhage on the ultrastructure of the myocardium of mice. *Am. Ht. Jr.*, 77: 427, March 1969.
2. Burch, G. E., Myers, R. and Abildskov, J. A.: A new electrocardiographic pattern observed in cerebral accidents. *Circulation*, 9: 719, 1954.
3. Cropp, G. J. and Manning, G. W.: Electrocardiographic changes simulating myocardial ischemia and infarction associated with spontaneous intracranial hemorrhage. *Circulation*, 22: 25, 1960.
4. Bryant, R. E., Thomas, W. A. and O'Neal, R. M.: An electron microscopic study of myocardial ischemia in the rat. *Circulation Res.*, 6: 699, 1958.
5. Reichenbach, D.: Heart injury following catecholamine release. *JAMA*, 208: 255, April 14, 1969.

On Schizophrenia

Freud was unable to treat schizophrenics with psychoanalytic techniques. He was unsuccessful in establishing a relationship with the psychotic individual that would allow him to verbalize his irrational hostility. In fact the more disturbed patients appeared to ignore any relationship. As a result, many researchers have concentrated on the search for biochemical factors in the disease.

Among biochemical evidences uncovered so far are that schizophrenics seem to have a defect in the metabolic processes by which the body normally breaks down and eliminates the neurotransmitters, adrenalin and noradrenalin. It is thought that in the schizophrenic the normal route of degradation of intermediate biogenic amines is blocked possibly because of missing enzymes. This they think might be the result of a genetic coding error and that toxic compounds having hallucinogenic properties similar to mescaline are produced in the body.

Another theory attempting to lay an organic basis for schizophrenia is the one proposed by Heath¹ of Tulane University School of Medicine, that an auto-immune reaction may cause antibodies in the blood stream of schizophrenics which attack certain specific regions of the brain. We know that noradrenalin and adrenalin are secreted during states of rage and anxiety. In an individual trained to inhibit any expression of negative feelings those products could build up in the schizophrenic. According to the theory just mentioned they could produce noxious substances that would impair the mental functioning.

There are serious difficulties in accepting a biochemical mechanism as the sole factor causing schizophrenia, which make these hypotheses hardly tenable. The apparent role of psychological stress in precipitating psychotic symptoms and the numerous examples of abrupt remission of psychoses in response to psychodynamic influence have always been difficult to explain with a purely biological model. As a result some have doggedly continued through the years to try and penetrate the problem of schizophrenia with a variety of psychological techniques but without encouraging results.

Dr. Hyman Spotnitz has now given us a hypothetical model of schizophrenia which seems to unify the two opposing points of view, the biological and environmental. Workers from a number of centers around the country reported last month at the American Orthopsychiatric Association that schizophrenia can be treated by Spotnitz's method and such patients have functioned normally for years without sign of relapse.

The new approach presumes that schizophrenia is a primitive defense against aggressive behavior developed by certain individuals who from birth are hypersensitive to external stimulation. When in infancy such an individual is discouraged by parental figures from expressing his reactions to things which irritate him, then schizophrenia may develop. Sometime during the first or second year of life these individuals unwillingly begin to employ the schizophrenic process including withdrawal from the real world and suppression of emotion to avoid experiencing intense feelings of frustration and rage. These threatening feelings can be triggered within the person prone to schizophrenia by seemingly trivial incidents that would cause only slight feelings of frustration in others.

Spotnitz's therapeutic approach consists of gradually leading the individual to become aware of the nature of the feelings he is trying to avoid and

to learn to express them verbally. This is a generalized form of psychoanalysis. By this means a schizophrenic patient who may initially have such psychotic symptoms as hallucinations can be brought to a point (after many years of therapy) where he functions normally and will not relapse with a psychosis. Unfortunately the successful psychotherapy of a schizophrenic represents a lifetime undertaking for a therapist. A minimum of five years is needed to produce significant progress and ten to fifteen years may be needed to assure immunity to psychosis.

With few patients treated, we do not know how many failures there might be after such prolonged treatment. With over two million schizophrenics, the method could hardly be applied to one in a hundred, and so drugs will no doubt continue to remain the most widely prescribed clinical treatment providing symptomatic relief for the great majority of schizophrenics. Occasionally they might even supplement the treatment of those undergoing psychotherapy.

The successful results achieved by psychotherapy, if further confirmed, heralds a new understanding of this disorder that should prove of enormous interest both to clinicians and in fields of academic research such as developmental psychology. The view that schizophrenic reactions develop out of experiences in the first and second years of infancy may shed more light on the normal developmental processes that take place during the early periods of life and can contribute much to our handling of children during these critical years of psychological and emotional development.

Many of the proponents of the two major historical points of view, the environmental and the biochemical now seem ready to embrace a unified model of schizophrenia, the one suggested by Spitz which recognizes an interplay between environmental and hereditary factors. In this model the schizophrenic is seen as being predisposed to the disorder because of heredity or even constitutional defects arising during intra-uterine life. The disorder then becomes manifest when such individuals are subjected to an unfavorable environment early in life.

The reports that early learning can be reversed by a favorable therapeutic environment, now renders the schizophrenic as a subject in whom to investigate the interactions of learning, primitive emotional responses, and the biochemical substrates of behavior.

L.H.N.

References

1. Heath, Russell: quoted by Scientific Research, 4: 29, May 12, 1969.
2. Spitz, Hyman: Modern psychoanalysis of the schizophrenic patient.
3. Davis, H. L.: Schizophrenia: A unified picture at last? Scientific Research, 4: 26, May 12, 1969.

Exercise, Propranol And Fibrinolysis

Biggs and her colleagues¹ reported long ago that vigorous exercise or the injection of adrenalin resulted in the appearance of spontaneous fibrinolytic activity in the blood of healthy volunteers. Since they found no such activity in the blood of resting subjects, they supposed that the phenomenon they found in the subject after vigorous exercise was a reaction of the body to stress. However, the word stress covers a variety of phenomena from adrenalin liberation, increased metabolites from muscular contraction, acceleration of blood flow through muscles and much else. As techniques for measuring fibrinolytic activity improved it became apparent that spontaneous fibrinolytic activity is also present in inactive persons and that both exercise and adrenalin seem to enhance a normal property of blood. Do they do this through the mechanism of adrenalin liberation alone or are there other factors besides the liberation of adrenalin operating to increase the fibrinolytic activity after exercise.

Recent information makes the latter proposition quite likely. Moderate exercise such as walking which is hardly stressful was shown also to increase fibrinolytic activity and other groups of workers have shown a relationship between the degree and duration of the fibrinolytic response to the distance walked. Currently a variety of evidence indicates that the spontaneous fibrinolytic activity of blood is due to an activator of plasminogen released from vascular endothelium mainly on the venous side of the circulation.^{2,3} This strongly suggests that the enhancement of fibrinolytic activity by moderate exercise is a reflection of increased blood flow through muscles, although none the less an important one for that.

This situation does not, however, preclude an adrenergic factor when exercise is vigorous and therefore stressful. Accordingly Cohen et al⁴ set out to determine the effect of strenuous physical exercise on fibrinolysis and blood coagulation and the role of beta-adrenergic receptors in mediating this response. When they blocked the beta-adrenergic receptors with propranolol it in no way altered

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the fibrinolytic response of healthy people to vigorous exercise. Additionally they found that propranol prevents the increase in the blood level of factor VIII which exercise ordinarily induces.

The increase in fibrinolysis is due to the increased plasminogen activation rather than to increased levels of circulating plasmin. Cohen is not alone in finding this enhancement of fibrinolysis since as we have seen above Biggs and her co-workers showed this many years ago. What she did show was that neither exercise nor propranol significantly alters the level of this coagulation factor or prothrombin time and thromboplastin time.

These findings are of more than academic interest. If as has been suggested natural fibrinolysis is a built-in fibrin clearing and hence antithrombotic mechanism, its enhancement should be beneficial to the organism and especially to patients with established or incipient occlusive vascular disease. We already know that exercise promotes collateral circulation. Thus we have added another beneficial factor that exercise benefits the circulation. It is therefore not surprising that there has been a turnabout of medical advice to patients

with ischemic conditions. No longer are they advised to adopt a sedentary existence.

On the contrary they are urged to take as much moderate exercise as is compatible with their symptoms. If as recent findings indicate, already existing defective fibrinolytic activity is commoner among survivors of myocardial infarction than among healthy people, and may have an adverse effect on prognosis, then we have additional support to encourage patients with coronary artery disease to exercise as much as possible.

But now comes the difficulty of angina pectoris for here the sanction against exercise is pain. Despite the value of nitroglycerin, its long acting derivatives have often proved disappointing in practice. The advent of propranol marks an important advance in treatment for it effectively increases exercise tolerance of patients with angina pectoris. It is therefore reassuring and encouraging to learn from Cohen and his colleagues that propranol does not as might be conjectured diminish the fibrinolytic response to exercise and moreover it prevents the presumably undesirable increase in factor VIII which attends exertion. Therefore propranol may do more therapeutically than simply to delay the onset of pain. By making more exercise possible, it can help promote a collateral circulation without interfering with the fibrinolytic response to exercise.

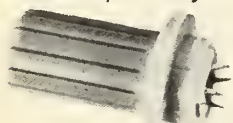
L.H.N.

References

1. Fibrinolysis, Exercise and Propranol. *Ibid.* p. 1283.
2. Kline, D. and Nahum, L. H.: Fibrinolysis I: Basic aspects of interest to the clinician. *Conn. Med.*, 24: 73, 1960.
3. Nahum, L. H., Kline, D. and Fishbein, R.: Fibrinolysis II: Evaluation of enzymatic thrombolysis: Experiments with plasmin preparations in arterial, venous thrombosis. *Conn. Med.*, 24: 139, March 1960.
4. Cohen, R. J. et al: Alterations of fibrinolysis and blood coagulation induced by exercise and the role of beta-adrenergic receptor stimulation. *Lancet*, II: 1264, Dec. 14, 1968.

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
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Some Complications of Intra-Uterine Contraceptive Devices

E. Marvin Henken, M.D., Mark Solomkin, M.D.,
Stanley W. Edelstein, M.D. and Benson Jay Horowitz, M.D.

Intra-uterine contraceptive devices (IUCDs) are presently in wide use. Most IUCDs are radiopaque and are often incidentally observed during radiographic examinations of the pelvis. Complications are frequent, and the radiologist is often called upon to localize the devices. It is the purpose of this paper to acquaint the physician with the more commonly used IUCDs and to demonstrate cases in which the radiologist helped localize the device.

History

The modern history of the devices has been summarized by Davis.¹ In 1928, Grafenberg⁴ described a rigid, metallic, wholly intra-uterine ring which required cervical dilation for insertion, but increased reports of perforation and infected abortions caused it to fall into disrepute, particularly in this country. With the advent of biologically inert materials, especially plastics, there was a resurgence of interest in the ring. In 1959, Oppenheimer⁵ reported a ring fashioned from silkworm gut, and Ishihama⁶ reported rings of both polyethylene and steel. In rapid succession other IUCDs were devised, emphasizing simple insertion and removal: Margulies⁷ utilized a preformed polyethylene spiral inserted through a straight cannula into the uterine cavity where it resumed its preformed spiral shape; Lippes⁸ used the same principle to insert a tapered double "s" shaped loop; Hall and Stone⁹ modified a stainless steel Grafenberg ring; Birnberg and Burnhill¹⁰ designed a bow or hourglass-shaped device which they felt would be more resistant to expulsion. Fig. 1 demonstrates two devices now commonly used.

Contraindications

Many investigators¹ have avoided IUCDs in nulliparous women because of the difficulties of insertion in a narrow cervical canal. In addition there

may be a tendency to blame infertility on the prior use of the device.

Medical contraindications include:^{1, 3} pelvic inflammatory disease, dysmenorrhea, myomata or previous myomectomy, hypoplastic uterus, endometritis, adenomyosis and menometrorrhagia.

Technique of Insertion

The devices are usually inserted immediately after menses or four to ten weeks postpartum, for

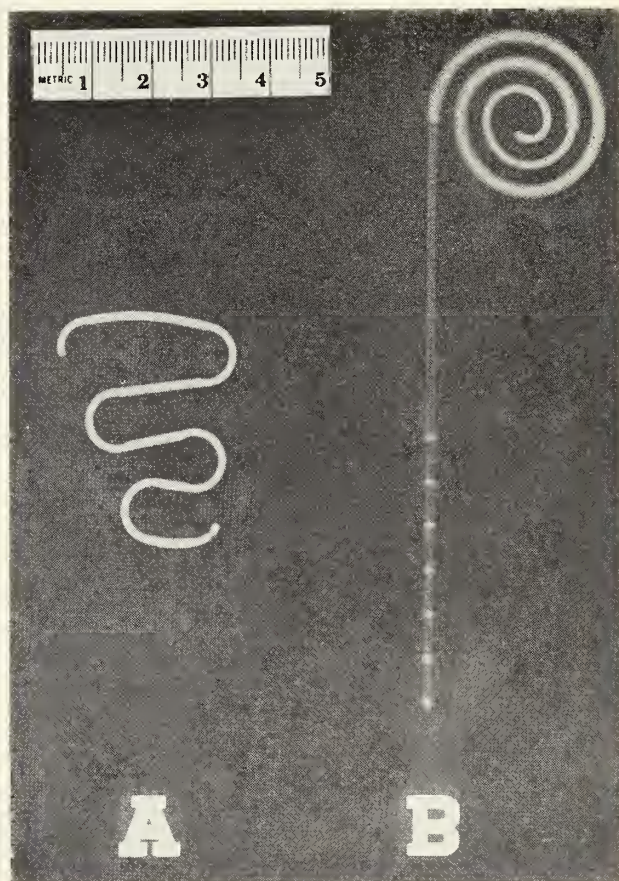


FIGURE 1

Roentgenogram of (A) Lippes loop, (B) Margulies coil.

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This study was aided in part by a grant from the Mark and Ruth Solomkin Foundation, Inc.

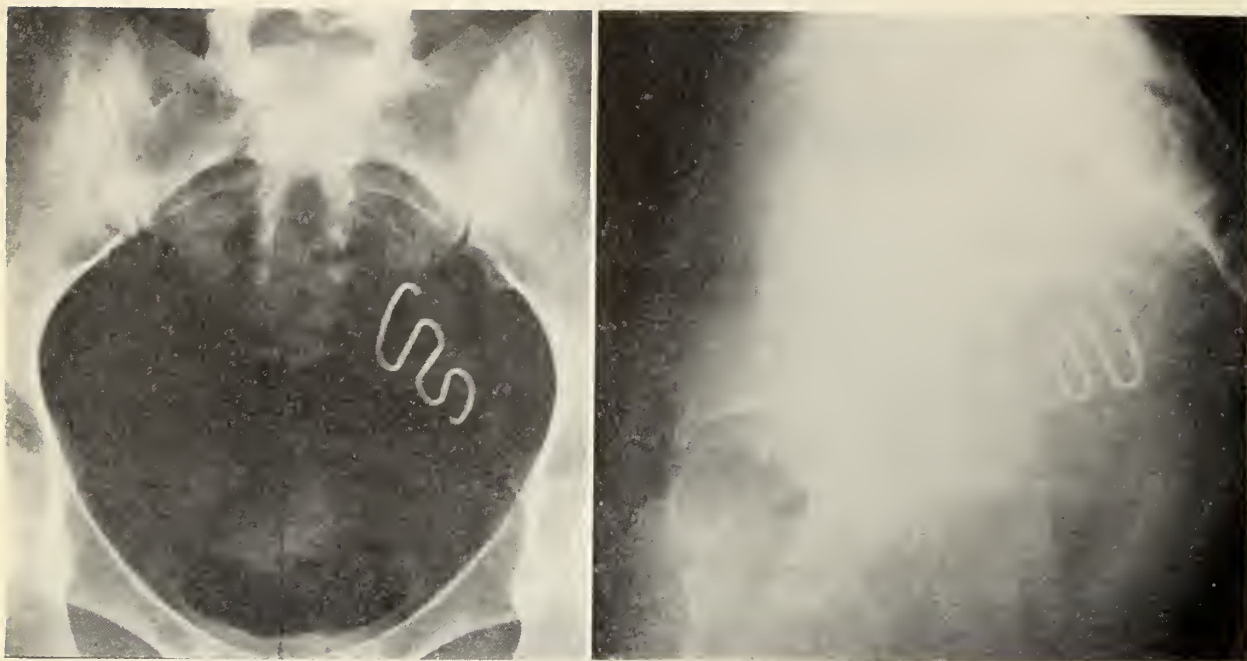


FIGURE 2

Anteroposterior and left lateral projection of the pelvis showing the IUCD high and posteriorly with its long axis slanting obliquely.

three reasons:¹ disruption of an unrecognized pregnancy is prevented; the cervical canal is already dilated; and complaints of cramps and spotting are minimized. After cleansing of the vaginal vault and cervix the uterine cavity is sounded to determine its length and axis. The tubular inserter containing the preformed plastic device is then inserted beyond the internal os and the device is introduced by a plunger. In the case of the rings a notched sound or special forceps is used for insertion. Most of the devices carry tails or fine plastic strings which protrude through the cervix to permit subsequent visual and/or digital confirmation of their presence. The patient returns after her first menstrual period to recheck the position of the device. Routine re-examinations including Papanicolaou smears are then performed at six to twelve month intervals.

Mode of Action

The mechanism by which the IUCD prevents conception has not been established. Most evidence indicates some interference with implantation of the ovum. Acceleration of tubal transport and/or endometrial changes may be contributing factors.^{1-3, 9}

Side Effects and Complications

The IUCD is a foreign body, and fear of a carcinogenic effect has been registered. In a study¹² of the uteri removed from 57 women who had IUCDs in situ for 1½ to 8 months, endometrial changes

ranging from edema to endometritis were observed, but a recent review² concludes that long term unfavorable results are unlikely.

After insertion, minor bleeding or spotting is common for a few days and some patients experience pelvic cramps. The more serious complications reported are:¹¹ infection; excessive bleeding and pain; embedding of the terminal bead of the tail in the vagina or cervical canal; IUCD embedded in uterine wall; fragmentation of the IUCD during attempts at removal; the IUCD ex utero.

The following case illustrates a uterine perforation demonstrated by X-ray.

CASE I. P. G. 25, gravida I, para I, had a Lippes loop inserted with considerable difficulty approximately 8 weeks after delivery. When examined 4½ weeks later, the strings were not visualized, and she stated she had "vaginal staining" every 3 to 4 days.

Roentgenograms of the pelvis (Fig. 2) revealed the IUCD in an unusual location.

During hospitalization, 1 week later, repeat roentgenograms were unchanged. Hysterosalpingogram (Fig. 3) confirmed the extra-uterine position of the loop. The device was easily removed through a posterior colpotomy.

Comment: Most perforations probably occur during insertion.¹ Since the devices are of relatively inert materials, perforations usually induce no symptoms. Therefore, the radiographic demonstration of an unusual position of the IUCD should lead to suspected perforation, and a hysterosalpingogram should be performed. Since the devices may

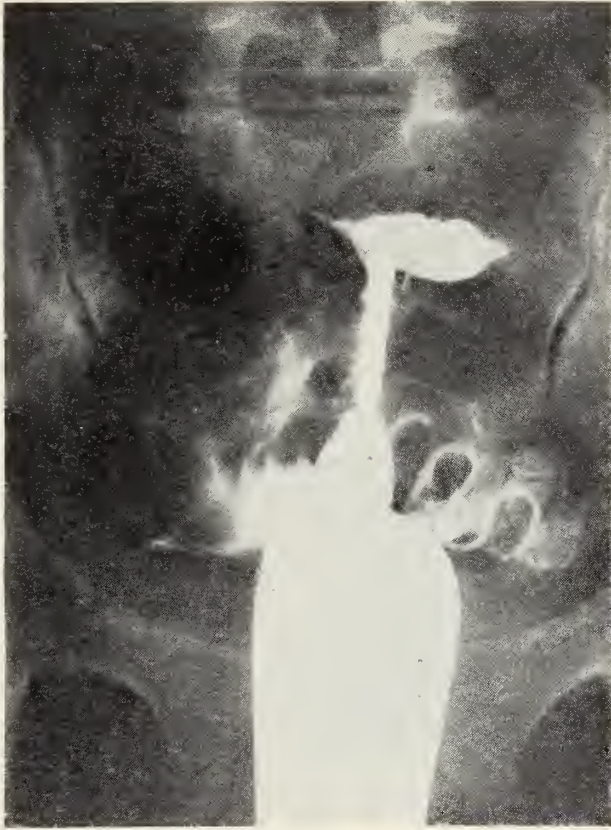


FIGURE 3

Hysterosalpingogram showing the IUCD free within the pelvis.

asymptomatically migrate within the peritoneal cavity beyond the pelvis, the entire abdomen should be included in the scout film when a device is being sought.

Results

This paper will not analyze the effectiveness of the IUCD or compare the various devices, but it has been reported¹ that 2% of the women become pregnant each year of exposure, with the device in situ. The incidence of complication and conceptions apparently are both the least in the Lippes loop.^{3, 11}

If pregnancy occurs, the device should not be removed if it has remained completely within the uterine cavity. However, there is a difference of opinion should the tail protrude through the external os. If spontaneous abortion does not occur, the device is usually delivered with the placenta.

Following are two instances of full term pregnancies involving two types of IUCD:

CASE II. R. G. 28, gravida IV, para IV, had a Lippes loop inserted eleven months after delivery. No problems were apparent for 6 months but she then reported her menses 2 weeks late. Examination revealed a pregnancy without evidence of any IUCD. Roentgenograms (Fig. 4) late in pregnancy demonstrated both the fetus and the device within the uterine cavity. Delivery at term of a 10 pound, 4 ounce male was uneventful, and the IUCD was recovered with the membranes.



FIGURE 4

Anteroposterior and left lateral view of abdomen demonstrating intra-uterine fetus and loop.

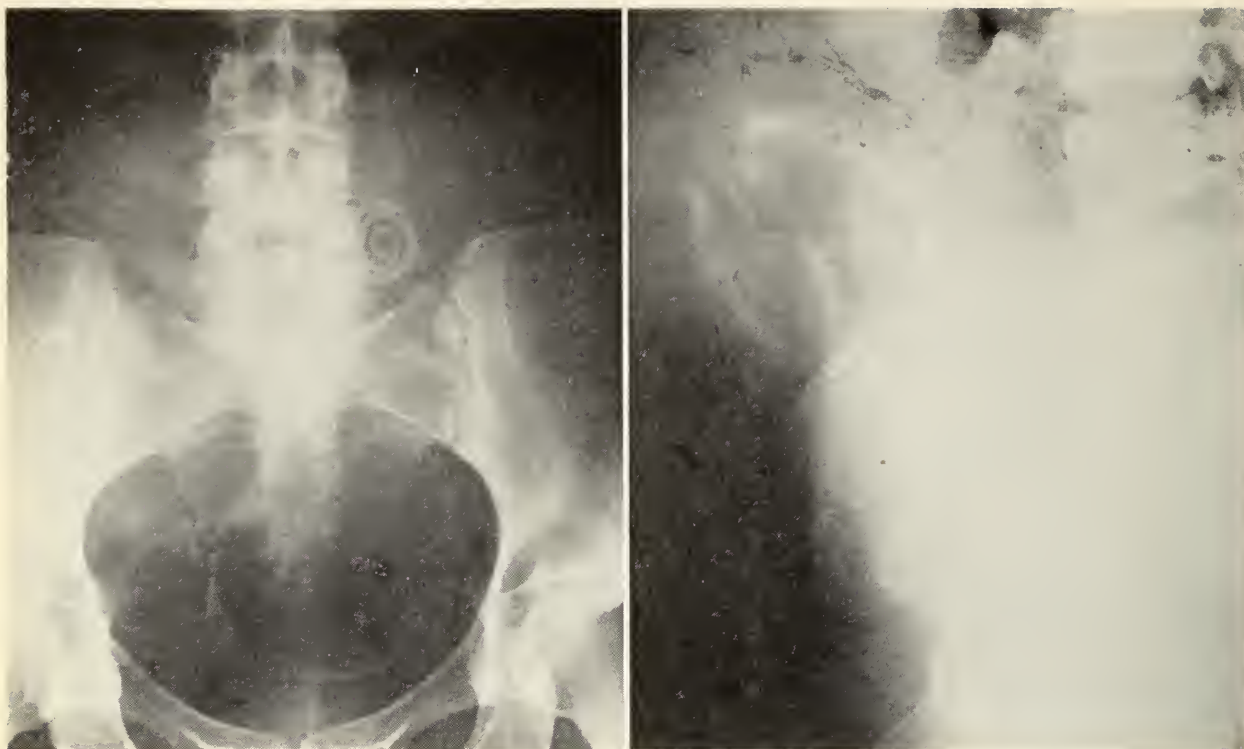


FIGURE 5

Anteroposterior and left lateral view of abdomen showing intra-uterine fetus and coil.

CASE III. H. S. 28, gravida III, para III, had a Margulies coil inserted 8½ months after delivery. No problems were apparent for 15 months at which time she reported her period overdue. Examination revealed a pregnancy without evidence of the device. Roentgenograms (Fig. 5) late in pregnancy revealed a fetus and the coil within the uterine cavity. At the uneventful delivery of a full-term 7 pound, 13 ounce female, the IUCD was recovered with the membranes.

Comment: When pregnancy occurs with the device in place, spontaneous abortion occurs with above average frequency^{1, 11} although many go to full term. To the authors' knowledge there have been no reports of increased incidence of fetal abnormalities in such cases.

Summary

A brief review of intra-uterine contraceptive devices is presented.

A radiographic search for the devices should be performed if the device is not palpable or visible after insertion, or if the patient is pregnant and the location of a previously inserted device is not known. Such an X-ray examination should include the entire abdomen.

References

1. Davis, H. J.: Status of Intrauterine Devices in Clinical Practice. *Current Med. Dig.* 33: 873-879, June, 1966.

2. Leading articles: Contraceptive Devices and Endometrium. *Brit. M. J.* 2: 1154, Nov. 12, 1966.

3. Nash, W.: Experience in Use of Intrauterine Devices for Contraceptive Purposes. *N.Y. State J. Med.* 65: 1872-1875, July 15, 1965.

4. Grafenberg, E. *Geburtenregelung* Berlin: Kurt Bendix, 1928. Cited by Davis (1).

5. Oppenheimer, W.: Prevention of Pregnancy by the Grafenberg Ring Method; a Re-evaluation after 28 years' Experience. *Am. J. Obst. and Gynec.* 78: 446, 1959. Cited by Nash (3).

6. Ishihama, A.: Clinical Studies on Intrauterine Rings, Especially the Present State of Contraception in Japan and the Experiences in the Use of Intrauterine Rings. *Yokohama Med. Bull.* 10: 89, April, 1959. Cited by Nash (3).

7. Margulies, L. C.: *Proceedings Conference Intrauterine Contraceptive Devices*, New York, 1962. Cited by Davis (1).

8. Lippes, J.: *Proceedings Conference Intrauterine Contraceptive Devices*, New York, 1962. Cited by Davis. (1).

9. Hall, H. H. and Stone, M. L.: Observations on the Use of the Intrauterine Pessary, with Special Reference to the Grafenberg Ring. *Am. J. Obst. and Gynec.* 83: 683-688, March 1, 1962.

10. Birnberg, C. H., and Burnhill, M. S.: A New Intrauterine Contraceptive Device. *Am. J. Obst. and Gynec.* 89: 137-138, May 1, 1964.

11. Hall, R. E.: A Comparative Evaluation of Intrauterine Contraceptive Devices. *Am. J. Obst. and Gynec.* 94: 65-77, Jan. 1, 1966.

12. Israel, R., and Davis, H. J.: Effects of Intrauterine Contraceptive Devices on the Endometrium. *J.A.M.A.* 195: 764-768, Feb. 28, 1966.

Psychiatric Consultation To A Teenage Unwed Mothers Program

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This is a report on the experience and observations of the Psychiatric Consultant to the Teenage Unwed Mothers Program at the Yale-New Haven Hospital, from July 1966 through June 1967. It emphasizes the limited self-awareness and limited psychological understanding of the lower class Negro girls who participated in the program, the difficulties that the psychiatrist encountered in interviewing them, and the importance of the psychiatrist's availability to the other clinicians whose daily work with the patients was the heart of the program.

There is an extensive professional literature¹⁻⁸ about the increasing rate of pregnancy and motherhood in teenage and out-of-wedlock groups, and about the proliferation of medical, educational and social services available to meet their special needs, but there are few reports of direct psychiatric participation⁹⁻¹⁴ in these studies or services. Osofsky *et al.* have recently described a multifaceted program similar to ours.^{13, 14}

The program at the Yale-New Haven Hospital¹⁵ was conceived and established by Dr. Philip Sarrel, an obstetrician. He had investigated the fate of the teenage primiparas who had babies out-of-wedlock under the care of the Obstetrical Clinic of this hospital in 1959 and 1960:¹⁶ by 1965 a high proportion of them had from three to five small children; they were not married, had not returned to school and were dependent on public welfare. The current program was founded on Dr. Sarrel's conviction that this self-perpetuating, destructive cycle could be interrupted through the provision of more intensive medical and social service. The program was started in 1965 as a separate unit within the hospital's pre-natal clinic. All unmarried New Haven residents under 19 who registered at the hospital for pre-natal care were invited to participate.

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The social worker got acquainted with each girl through regular individual interviews and through visits to her home and family. She met weekly with groups of six to ten girls, who were at approximately the same stage of pregnancy, to discuss pregnancy, sex, marriage, parents, school, jobs, race, etc. The social worker also saw some of the girls' boy friends, and she worked closely with the social agencies that were involved with individual girls.

The obstetrician saw each girl for regular prenatal care and for individual counseling. He joined the social worker in those group sessions that dealt with bodily changes during pregnancy, labor and delivery, the menstrual cycle, conception and contraception. He established a warm relationship with each girl and deliberately attempted to fill a paternal role that was missing in most of their lives. He was firm in encouraging each one toward completion of her education, toward marriage where possible, toward use of contraception and toward a generally optimistic outlook. He emphasized the positive aspects of motherhood and the importance for each girl of accepting her maternal role and maternal identity. "Now *you* are going to be a mother," he would tell each girl, "This is going to be *your* baby and *you* must take care of it." While he recognized the immaturity of most of the patients, he felt this support of the maternal role was essential to help them find strength, increased maturity and self-respect in their new responsibilities.

The obstetrician's concern with the general problems of pregnancy in young unmarried girls and his interest in the individual girls enabled him to discuss their problems with them without moralizing or condemning. His personal involvement and his belief in the importance of continuity in his relationship with each patient led him to be available to them by telephone 24 hours a day and to deliver almost all of their babies himself. He encouraged the babies' fathers to come to the hospital

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while the patient was in labor, and he made himself available to the fathers for counseling.

The personal continuity of care extended into the post-partum period as long as the individual staff members remained in the program.

The work of the psychiatrist included direct participation with the few most disturbed girls, consultation with the other clinicians and with the school, welfare and community agencies, and participation in planning the service and research aspects of the program. His work will be best understood after the characteristics of the patient population are presented.

Characteristics of the Patient Population

Although the potential research value of the program was recognized from the outset, plans for systematic, prospective data gathering were not organized or funded until the second program year. The data which follow were collected retrospectively at the end of the second year from the hospital records and from the social workers' notes and their knowledge and impressions of the patients. Although over 100 girls were participating in the program, the data presented here covers only the 80 who delivered, between September 1, 1966 and August 31, 1967.*

The patients ranged in age from 13 to 19 by the time of delivery. The majority were 15 to 17. All but two were Negro. Over half were born in the south, mostly in North and South Carolina. One third were born in New Haven.

The composition of the homes where the girls resided was generally consistent with other studies of the lower class urban Negro.¹⁷ Only one quarter of the girls' fathers lived in the home; in another quarter some other adult male relative was identified as head of the household. For half of the patients, therefore, a woman heads the family, usually the patient's mother, who is still young, sexually active and producing children of her own. The majority of households include one or more children younger than the patient: if not siblings they are

usually children of siblings. During a measured 18 month period surrounding each girl's delivery we know of one-third as many pregnancies among the mothers and sisters of the patients as among the patients themselves. Contrary to many sociological descriptions of this segment of society, the presence of a grandmother is reported in only very few of our patients' homes.

We have not yet gathered data on the meaningful informal details of these girls' home lives or friendships. In general they lived in crowded apartments, inevitably sexually provocative, with beds in every room but the kitchen. One of the social workers reported that when she made home visits she frequently had to walk through a room in which someone was sleeping. She never saw a family sitting down to a meal together, or even preparing a full meal, and was never invited to have a cup of coffee although there was no doubt that the patients liked her. The impression was gathered that people drifted in and out of these homes to eat or sleep or watch television. The many babies seemed to be fed when hungry.

Our teenage patients, already chronically deprived, usually cared for the younger children in the home while their mothers were out working or playing. Patients were often heard to say, "I got tired to taking care of all of my mother's children. I wanted to have one of my own." Some said, "Being pregnant and having a baby is the only way that I can feel grown up and can amount to anything." Although many mothers chastise their daughters for their sexual behavior, the mother may take care of the teenager's baby while the younger mother is away from home, at school, work or play. Some of the girls complain that their mothers take their babies away from them in this way; they are quite ambivalent about the possibility that the baby could grow up not knowing who its mother really is. There are many children in this population raised in the belief that they are the younger siblings of their true mothers.

We do not have complete data as to whether the patients and their close relatives were born in or out of wedlock, nor as to the degree of promiscuity or extent of sexual experience among the patients. Several families were represented in the program by more than one patient. There were several instances of a girl purposely getting pregnant because her best friends were pregnant, and some were pregnant by the brothers of other girls in the program. Most of the putative fathers were within a year or two of the girl's age.

* The collection and analysis of these data were made possible by grants H-118 and H-231 from the Children's Bureau, Department of Health, Education and Welfare.

The authors wish to express their appreciation to Susan Trimble, Joyce Levine and Catherine O'Hare of the Social Work Staff for permission to use information which they collected; to Barbara Cohen and Thelma N. Thornton of the research team for their help in data tabulation, and to Dr. Lorraine V. Klerman, Study Director under the Children's Bureau Research Grant, for her editorial help with the data and the manuscript.

Only a few of the girls had adequate understanding of reproductive physiology. Many did not know how intercourse causes pregnancy. Their knowledge of contraception was minimal. They blamed their families for not teaching them the facts of life and for not exercising stricter control over their behavior. In general they welcomed the rules and advice, and the instruction about themselves and about society, that the staff gave them.

The Task of the Psychiatrist

This program was founded with the explicit purpose of interrupting a self-perpetuating cycle of psychological and social distress and dependence. The psychiatrist, like the rest of the staff, was eager to help the patients with their severe problems, but individual consultation with the psychiatrist was not easily accepted by the patients and was not a large part of the program. The same factors which make these girls high obstetrical risks and high psychiatric risks also make them poor candidates for the standard psychotherapeutic approach which requires that they initiate discussion of their own feelings and conflicts. Just as the obstetrical program had to be adapted from the usual clinic style to a more personal continuity, so the psychiatric approach had to be modified in order to be useful to the patients. The patients' understanding of themselves and their lives is concrete and practical. They are not accustomed to thinking in terms of feelings and conflicts except in the broadest sense. This is manifested in their limited emotional vocabularies. It is hard for them to identify their feelings more exactly than to say e.g., "I was upset" or "That bothered me a lot" or "He's so aggravating." They need active help in recognizing and expressing their feelings, in much the same way that they have to be taught about their sexual anatomy and about contraception.

When offered the opportunity to see the psychiatrist many of the patients replied, "I don't want to have my head examined" or "I'm not crazy." While they are probably saying what they mean, we believe that these words have additional meanings for them. We presume, for instance, that these phrases are as close as they can come to expression of their fear that the white psychiatrist will read their minds, criticize them for their troubled feelings and resentments, their yearning for love and their sexual behavior. If they can be helped to find more accurate words for these feelings they could begin to come to grips with the problems of their lives.

In a more effective position than the psychiatrist to help the girls recognize and deal with their feelings were the obstetrician, social workers, nurse, school teachers and pediatrician. The girls met with them week after week around the practical issues of pregnancy and motherhood and developed considerable comfort and trust with them; they then became able to discuss their friendships, families, worries, plans and hopes. Group participation with peers increased the girls' comfort and facilitated their discussion of important personal matters; individual interviews and group meetings complemented each other. In our program as in others^{18, 19} this kind of group therapy has been especially helpful in bridging the gaps in understanding and experience that separate the doctor or social worker from the reticent lower class patient.

The psychiatrist joined the program at the end of its first year. During the following year, 1966-67, he saw many of the patients briefly with the other clinicians and saw eight patients in extended individual consultation. His principal work was in his day by day discussions of clinical problems with the obstetrician, the social worker and the pediatrician and in the weekly clinical conferences with them. All members of the team were eager to understand the relationships and motivations of the patients' lives and to extend their clinical awareness and clinical skills. As a result the working relations among staff members and between staff and patients were generally quite satisfying. The psychiatrist's orientation was to a clinician-centered consultation²⁰ in which he helped the other clinicians to manage clinical problems as they arose with patients; he did not usually take over the management of the problems himself. He was often able to identify covert feelings and covertly manipulative behavior with which patients were making staff members feel uneasy, guilty, incompetent or competitive. He used his knowledge of psychodynamics and psychopathology to explain patients' behavior and feelings to the other clinicians and he advised the clinicians on interviewing techniques for eliciting information and for helping a patient to identify and come to grips with her own problems. The resulting frank discussions about painful and embarrassing topics helped the staff to discover that people are not as fragile as they seem and that the best solutions to a patient's problems are usually found when the patient is included in the discussion and is expected to share in the responsibility for finding solutions. The psychiatrist

also supported his colleagues in resolving intra-staff difficulties through direct and open discussion.

By the time that a formal psychiatric referral took place there had been extensive discussion among all parties involved and the patient and staff had a pretty clear idea of what the psychiatrist thought he could do to help. In some cases the social worker or obstetrician sat in with the patient during her first interview with the psychiatrist. This was not only reassuring to the patient but also gave the other clinician a direct experience with the psychiatrist's technique and style. When the patient came alone to the psychiatrist she was characteristically shy and guarded until the psychiatrist told her that he knew of the reason for the referral and inquired about her feelings about coming to see him. Most of the girls could acknowledge some nervousness at this point, but could not easily elaborate on their problems or troubled feelings. Discussion of practical everyday matters of the girl's life helped to put the girl at ease and gave the psychiatrist and the patient a common basis for further discussion. In this way the patient repeated with the psychiatrist the building of trust and confidence that she had already experienced with the other clinicians in the program. It proved helpful to ask what the patient does for fun as well as what her greatest problems are; it demonstrated that the psychiatrist was interested in understanding the total picture of the girl's life and not just her inadequacies.

We do not have enough information to differentiate the problems or personalities of all of the eight girls seen in psychiatric consultation from the total population of 80 girls delivered or the 100 girls participating in the program. We can say some things about them, however. All of the girls seen by the psychiatrists were significantly depressed, and most of them had borderline or frank psychotic experience. Whereas one quarter of the total group of 80 reported that their fathers were at home, none of this group of 8 lived in the same household with her father; two of the 8 were wards of the State. The only two white girls in the program were seen by the psychiatrist and the only thirteen-year-old was seen. Of the seven girls who became pregnant again after participation in the program, three were referred to the psychiatrist, one before and two after becoming pregnant again. Most of the eight terminated their contact with the psychiatrist after three to six visits; they all continued their active participation in other aspects of the program, however, which permitted con-

tinued indirect psychiatric consultation, through the other clinicians.

Obstetrical Results

Sarrel and Klerman have reported elsewhere²¹ on the much lower obstetrical morbidity experienced by the participants in this program than would be expected from the same population utilizing standard pre-natal clinic services.^{2, 5, 7} These findings are consistent with those of other programs similar to ours.^{1-6, 13}

Only seven of the 100 girls became pregnant again during the first two years of the program (1965-67). This compares favorably with earlier figures gathered by Sarrel and Davis from this hospital:¹⁶ among 63 out-of-wedlock primiparas of 1963, 36 delivered second children in 1964; and of 100 unwed primiparas delivered in this hospital in 1959-60, 95 had further pregnancies, producing 240 additional children by 1965.

Discussion

The problems of unmarried pregnancy and motherhood in teenagers are by no means limited to lower class Negroes (see bibliography compiled by Savitz *et al.*³). The incidence is rising rapidly among all social classes, and most rapidly among middle class white girls. It is well documented, however, that white girls and middle and upper class girls of all races in this country usually deal with unwed pregnancies through maternity homes, private medical care, adoption or abortion.^{1, 7, 22} This is also true in New Haven. The many white girls who were eligible for our program elected to use other facilities that were not realistically available to the Negro girls we served. (cf.⁴).

The psychiatric studies of young unmarried mothers,^{8-12, 14, 22, 23} emphasize severe early deprivation, severe disturbance of family relationships and impulsive response to intra-familial and intra-psychic pressures; Fleck⁹ emphasized their resultant incompetence in the new mother role. The personal experience of low self-esteem, humiliation, emptiness, and rage are described in most of the clinical accounts of young unwed mothers. These are also the characteristic experiences of the lower class in general, the mentally ill, and the oppressed Negro, as described by sociologists and by psychiatrists.^{17, 24-27}

Within the structure of our program we have not focused on the psychopathology of our patients and we have had only limited success in exploring their inner emotional experience. What we have learned of their lives and what they have been able

to tell us of their feelings indicates clearly that their psychological development is impoverished. They are poorly equipped to deal with the tasks of adolescence, let alone adulthood and motherhood. That they are young, immature members of a racial minority, many of whom have been separated from important ties with their wider families in the South, is only the background of their dilemma. Over half of them have grown up without a father or a stable father image and therefore have little or no realistic concept of an adequate adult male or of a marriage relationship based on mutual respect and affection. Their mothers have also been over-burdened and deprived and unable to meet our patients' need for love; they have added insult to injury by giving the girls younger siblings to take care of. Competing with their siblings and their mothers, having no experience of a settled home life or stable family relationships, seeking peer group acceptance, acting out their resentments against their seemingly uncaring parents, and desirous of creating something of their own to love, to care for and to control, the girls seek pregnancy or at least they permit it to occur.

Although Leffeldt's concept of Willful Exposure to Unwanted Pregnancy (WEUP)²⁸ was coined for educated middle class women who were quite knowledgeable about contraception, there is strong evidence that similar motivations were at work in the pregnancies that brought these patients to our program. Most of our patients had not seriously considered the prospect of raising a child and are not prepared for this responsibility. The wish to become pregnant or to have a baby is usually isolated in their minds from the consideration that the baby will grow up. Child care ties them down, interferes with their schooling and their hopes for self-improvement. Their needs for love and care are further frustrated and their resentments are deepened. A girl's chance of developing an adequate, self-sustaining personality structure amidst these conflicts is very small. Some of the girls seem to relate to their babies on the level of a five year old who feeds her doll and has the doll hug her to help herself over her jealousy of her mother's new baby.

The program we are discussing attempts to intervene in this complex psycho-social problem in several ways. The core of the program is the continuity of relationships between individual staff members and individual patients, and the use of these relationships to help the girls come to grips with their problems, increase their self-esteem and

take charge of their own lives. The clinical relationship in this non-psychiatric setting is used in much the same way that the clinical relationship is used in psychotherapy: it meets the patient on her own terms, without moralizing, invites trust, maintains appropriate distance and encourages the patient's self-reliance.

More specifically, the obstetrician explicitly attempted to strengthen the patient's positive identity as a mother and to strengthen the mother-child unit. He sees this approach as essential to emotional maturation of the young mother and to the new child's emotional security. He urged his patients to avoid falling into the role of siblings to their new babies, for he feels that supports the negative and undesirable aspects of young motherhood rather than the strengthening and maturing aspects. He carried it further by encouraging the patients' interest in seeking further education, stable marriage and economic security.

The obstetrician thus became a more satisfactory male model than most of the girls had previously known. The nurse, who was the only Negro on the clinic staff, and the social workers provided very positive feminine models. In making himself available to the putative father as well, the obstetrician seemed to have a strengthening effect on the self-esteem of the boy and on the relationship between the boy and girl. There was evidence that many of these couples cared a good deal for each other but were too caught up in individual defensive and competitive attitudes to be able to sustain a close relationship without considerable help. Most of this help came from the obstetrician, social workers, nurse, community workers and school teachers, although a few of the couples were seen together briefly by the psychiatrist.

With appropriate help many of these young people demonstrated their ability to handle their feelings and interpersonal relationships quite adequately. They needed to learn about themselves, and to learn new ways of getting along. They also needed to learn about their bodies, in particular about reproductive physiology and about contraception. In general they proved quite able to make good use of this kind of knowledge, as well. In the supportive setting of their special school they were able to carry on their formal education quite adequately. In many ways then, this program helped them to mature and to learn new skills appropriate to adolescence and to begin to make up for deficits in their own deprived development. The very low rate of repeat pregnancies in the program and the

widespread increase in self-respect and life satisfaction among the participants suggest that important needs were being met in ways that made pregnancy less necessary.

Bibliography

1. Teele, J. E., Robinson, D., Schmidt, W. M., and Rice, E. P.: Factors Related to Social Work Services for Mothers of Babies Born Out of Wedlock, *Am. J. Pub. Health* 57: 1300-1307, 1967.
2. Anderson, U., Jenss, R., Mosher, W. E., and Richter, V.: The Medical, Social and Educational Implications of the Increase in Out-of-Wedlock Births, *Am. J. Pub. Health* 56: 1866-1873, 1966.
3. Savitz, R. A., McCann, M., and Stitt, P. G.: Childbearing in and Before the Years of Adolescence (A Selected, Annotated Bibliography Covering 1960 to May 1965), Washington, Children's Bureau, Welfare Administration, U.S. Dept. of Health, Education and Welfare, 28p., 1966.
4. Herzog, E., and Bernstein, R.: Health Services for Unmarried Mothers, Washington, Children's Bureau, Welfare Administration, U.S. Dept. of Health, Education and Welfare, 61p., 1964.
5. Hassan, H. M., and Falls, F. M.: The Young Primipara: A Clinical Study, *Am. J. Obst. & Gynec.* 88: 256-269, 1964.
6. Israel, S. L., and Woutersz, T. B.: Teenage Obstetrics: A Cooperative Study, *Am. J. Obst. & Gynec.* 85: 659-668, 1963.
7. Pakter, J., Rosner, H. J., Jacobziner, H., and Greenstein, F.: Out-of-Wedlock Births in New York City I—Sociologic Aspects, *Am. J. Pub. Health* 51: 683-696; II—Medical Aspects, *Am. J. Pub. Health* 51: 846-865, 1961.
8. Vincent, C. E.: Unmarried Mothers, New York, Free Press of Glencoe, 308p., 1961.
9. Fleck, S.: Pregnancy as a Symptom of Adolescent Maladjustment, *Int. J. Soc. Psychiatry* 11: 118-131, 1956.
10. Mahnquist, C. P., Kiresuk, T. J., and Spano, R. M.: Mothers with Multiple Illegitimacies, *Psychiatric Quart.* 41: 339-354, 1967.
11. Kravitz, H., Trossman, B., and Feldman, R. B.: Unwed Mothers, Practical and Theoretical Considerations, *Canadian Psychiatric Association Journal* 11: 456-464, 1966.
12. Cattell, J. P.: Psychodynamic and Clinical Observations in a Group of Unmarried Mothers, *Am. J. Psychiat.* 111: 337-342, 1954.
13. Osofsky H. J., Hagen, J. H., and Wood, P. W.: The Program for Pregnant School Girls. Some Early Results, *Am. J. Obst. & Gynec.* 100: 1020-1027, 1968.
14. Osofsky, H. J., Hagen, J. H., Braen, B. B., Wood, P. W., and DiFlorio, R.: Problems of the Pregnant School Girl. An Attempted Solution, *New York State J. Med.* 67: 2332-2343, 1967.
15. Sarrel, P. M.: The University Hospital and the Teenage Unwed Mother, *Am. J. Pub. Health* 57: 1308-1313, 1967.
16. Sarrel, P. M. and Davis, C. D.: The Young Unwed primipara, *Am. J. Obst. & Gynec.* 95: 722-725, 1966.
17. Rainwater, L.: "Crucible of Identity: The Negro Lower-Class Family," in "The Negro American—2", *Daedalus (Journal of the American Academy of Arts and Sciences)* 95: no. 1, 1966. (See also the other articles and bibliographies in that issue and in *Daedalus* 94: no. 4, 1965.)
18. Beck, J. C., Bottenweiser, P., and Grunebaum, H. U.: Learning to Treat the Poor: A Group Experience, presented at the American Group Psychotherapy Assn., 24th Annual Conference, New York City, January 26-28, 1967.
19. Roemele, V. & Grunebaum, H.: Helping the Helpers, *Int. J. Group Psychotherapy* 17: 343-356, 1967.
20. Schiff, S. K., and Pilot, M. L.: An Approach to Psychiatric Consultation in the General Hospital, *A. M. A. Archives of General Psychiatry* 1: 349-357, 1959.
21. Sarrel, P. M., and Klerman, L. V.: The Young Unwed Mother—Obstetrical Results of a Program of Comprehensive Care, mimeographed, Presented at the District Meeting, American College of Obstetrics and Gynecology, Las Vegas, Nevada, October 25, 1967.
22. Young, L.: Out-of-Wedlock, New York, McGraw Hill, 261p., 1954.
23. Gough, D.: Understanding Unmarried Mothers, Observations of a Psychoanalyst, London, National Council for the Unmarried Mother and Her Child, 16p., 1966.
24. Hollingshead, A. B., and Redlich, F. C.: Social Class and Mental Illness: A Community Study, New York, Wiley, 442p., 1958.
25. Oltman, J., and Friedman, S.: Parental Deprivation in Psychiatric Conditions: III. In *Personality Disorders and Other Conditions, Diseases of the Nervous System* 28: 298-303, 1967.
26. Kardiner, A., and Ovesey, L.: The Mark of Oppression, Explorations in the Personality of the American Negro, Cleveland, Meridian-World Publishing Co., 396p., 1962.
27. Coles, R.: Violence in Ghetto Children, *Children* 14: 101-104, 1967.
28. Lehfeldt, H.: Willful Exposure to Unwanted Pregnancy (WEUP), Psychological Explanation for Patient Failures in Contraception, *Am. J. Obst. & Gynec.* 78: 661-665, 1959.

Recent Thoughts On Psychosurgery

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This short paper constitutes an informal discussion of the present uses of psychosurgery in the treatment of psychiatric illnesses.

With the advent of newer drugs in the 1950's psychosurgery approached extinction as a mode of formal therapy. In the late 1960's it has returned to favor as a mode of treatment in certain intractable cases of mental and emotional disease failing to respond to psychotherapy, tranquilisers, and short courses of shock therapy. Fractional or selective lobotomies have replaced the original complete lobotomy.

Case Selection

DEPRESSIONS continue to give the best results and should be done in those cases requiring more than one or two courses of electric shock; in elderly people; in those patients with epileptic tendencies, and in those patients having recurrences. More than one to two courses of shock treatment probably causes more diffuse brain damage than the newer fractional lobotomies.

ANXIETY TENSION STATES: Fractional lobotomies give excellent results in these conditions and unexpectedly are of even greater benefit in those agitated anxiety states of the aged suffering from insomnia, agitation and depression.

Rare cases of alcoholism, when resulting from an attempted escape from anxiety, can be benefitted.

INTRACTABLE SOMATIC CONVERSION NEUROSES WITH HYPOCHONDRIASIS do exceptionally well and may be dramatically relieved. Concomitant drug addiction in such patients is equally benefitted.

SEVERE OBSESSIVE COMPULSIVE NEUROSES are intractable to most forms of therapy especially shock treatment. They show moderate benefit from selective lobotomy. They continue to show an underlying rigid and obsessive personality but the obsessions are brought under control and the patients frequently can return to productive living.

PSEUDONEUROTIC SCHIZOPHRENIA: On the surface such patients resemble a severe obsessive compulsive or hysterical intractable neurotic but psychometric survey and prolonged study reveal the presence of an underlying schizophrenic state. To our surprise, such cases show excellent late results following fractional lobotomies. The underlying schizophrenic bizarre thinking and delusions may be brought to the surface causing some concern to the relatives but the increased ventilating and the ability of the physician to make better contact seems to take the sting out of these delusions, and over the years the results have been very favorable.

PAIN: Selective lobotomy is contra-indicated in cases of organic pain such as metastatic disease of the spine but is of distinct value in those terminal cases of cancer where the anticipation of pain, the fear of impending death, and the memory of pain are the predominant disabilities. The resulting addiction is also alleviated.

Type of Operation

Orbital undercutting interrupts the connections from the orbital cortex of the frontal lobes to the thalamus. It constitutes a physiologic isolation of the under surface of the frontal lobes anterior to the sphenoid ridge and medially anterior to the transverse portion of the anterior cerebral arteries. It is advocated in preference to medial quadrant leukotomies of McKenzie; of Poppen; of Grantham and Mayfield; and the cingulectomies of Le Beau; Livingston; and Ballantine because the quantitative sectioning of connecting fibers can be exactly duplicated from case to case under direct vision and measurement. The other methods constitute a blind approach with partial sectioning of converging fibers under the frontal horns with inevitable variations in the amount resected from case to case.

Over the years it has become clear that inferior medial quadrants are the most important areas for therapeutic benefit so that superior convexity resections are no longer used.

The writer takes polite issue with the concepts of Ballantine, Le Beau and Cairns on the relation of the anterior cingulate area to mental disease.

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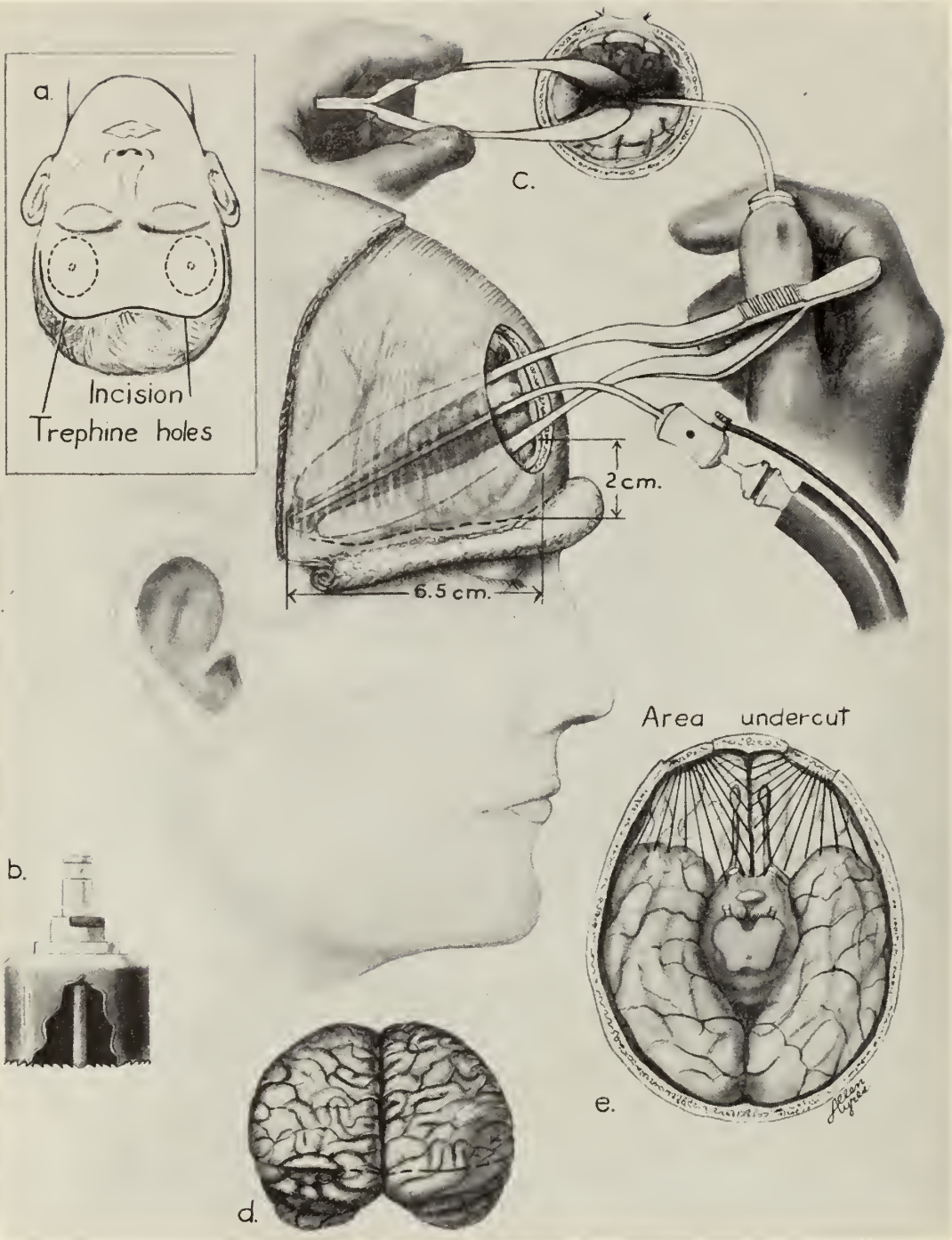


FIGURE 1

Sketch of Surgical Technique of Orbital Undercutting.

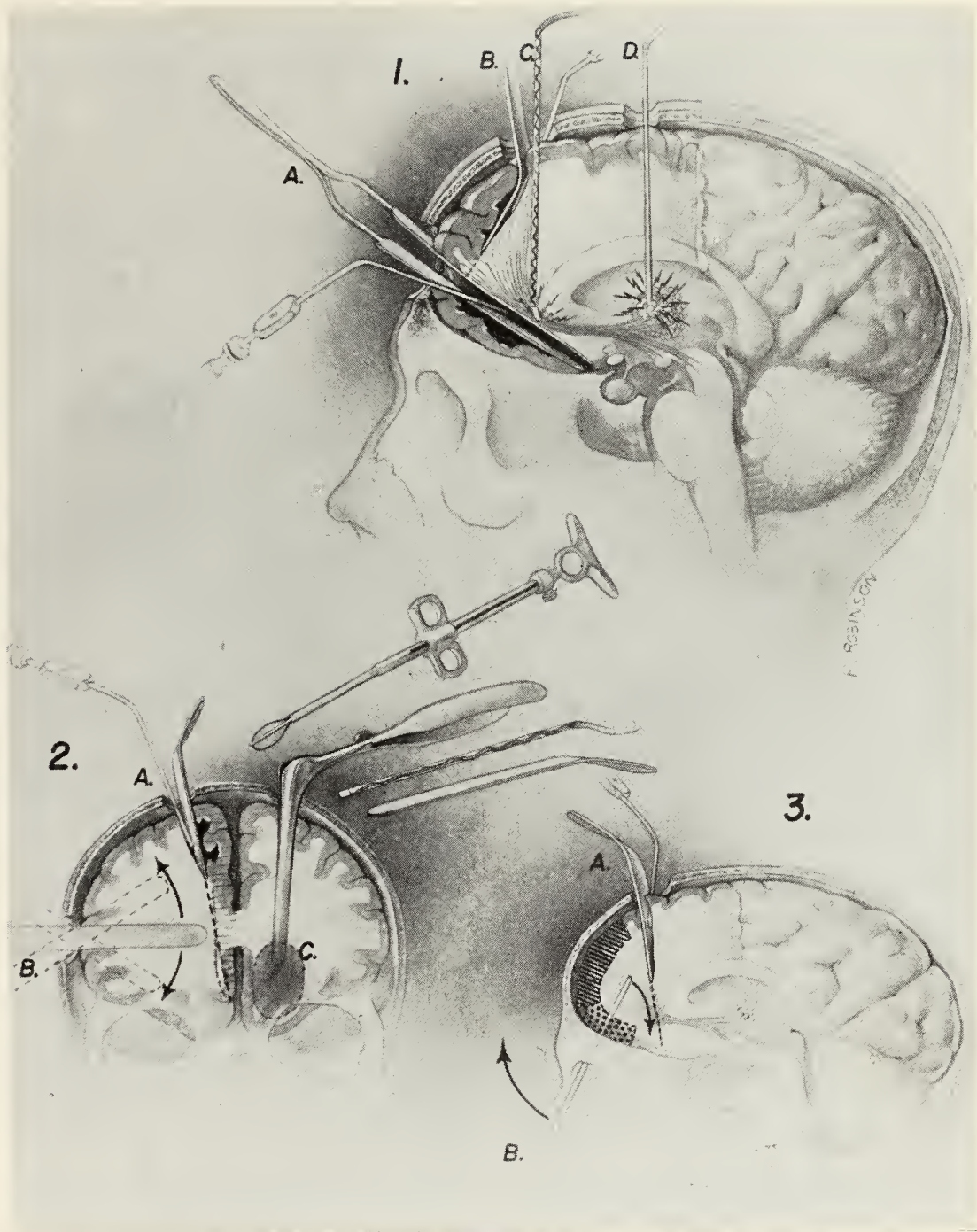


FIGURE 2

- 1A Orbital Undercutting (Scoville)
- 1B Undercutting of the superior convexity (Scoville)
- 1C Inferior quadrant leukotomy (Grantham, electrical)
- 1D Thalamotomies
- 2A Undercutting of rostral cingulate gyrus (Scoville)
- 2B Standard closed lobotomy (Freeman and Watts)
- 2C Instruments used in inferior quadrant leukotomy (Loupe of McKenzie; speculum, electrocautery of Grantham; spatula of Poppen)
- 3A Standard open lobotomy (Poppen)
- 3B Transorbital lobotomy (Freeman)
- 3 Cross hatch and dotted lines indicate areas of topectomy (Pool)

The writer concurs that the so-called cingulectomies have shown appreciable benefit but believes the benefit results from blind interruption of underlying white matter adjacent to the cingulate cortex, which contains those converging fibers from the entire prefrontal lobe. The anterior cingulate cortex is not sensitive to stimulation and its discrete removal has no measurable effect on the vital signs nor the psyche as found by Kahn, German, and the writer.

Orbital undercutting should be extended well posteriorly to a level slightly behind the optic chiasm. Stress is made on the necessity of remaining close to grey matter at the posterior limits of the undercutting for if one gets into the septal area and anterior hypothalamus a confusional state and temporary deterioration may result.

Discussion

It is apparent to this writer that different types of mental disease do not require different areas of ablation or tract interruptions. There appears to be no need to vary the location of operation in the neuroses, cyclical depressions and schizophrenia.

Ablations of inferior portions of the prefrontal lobe appear to affect mood and of the superior areas to affect higher intellectual faculties. Consequently inferior sectioning is preferable.

All prefrontal lobe surgery probably benefits by a blunting of function. Therefore lobotomy is applicable to those diseases exhibiting exaggerated emotional tension, anxiety, conscience, phobias, or thought distortions because a blunting of such symptoms will be of benefit. Lobotomy is not of benefit in constitutional psychopathic personalities, constitutional criminals, and those patients suffering from sexual or constitutional amorality. Social alcoholism is not benefitted.

Lesions in the deeper midline structure frequently affect the psyche and states of consciousness,

more particularly those regions of the reticular, limbic, hypothalamic, and mammillary areas. Unfortunately lesions in these areas tend to cause rather than relieve the majority of psychotic states, especially confusional, catatonic, schizophrenic, and Korsakoff's states. Aneurysm surgery, especially of the anterior communicating artery, tends to confirm this.

Post-operative seizures do not constitute a social problem except following topectomy.

Prophylactic Dilantin prevents the majority of seizures and those few seizures which do occur are generally nocturnal and in bed.

Conclusions

1. Limited lobotomies continue to offer satisfactory relief in those intractable depressions, neuroses, psychic pain, and certain schizophrenias, which do not respond to the newer drugs.

2. Orbital undercutting offers certain advantages over other inferior quadrant surgical, chemical, or electrical "closed" operations because of its measured precision under direct vision permitting precise removal and duplication from case to case.

Bibliography

Scoville, W. B. Selective Cortical Undercutting as a Means of Modifying and Studying Frontal Lobe Function in Man. *J. Neurosurg.* VI, 65-73. 1949.

Scoville, W. B. Selective Cortical Undercutting: Results in New Method of Fractional Lobotomy. *Am. J. Psych.* 107: 730-739. 1951.

Scoville, W. B., Dunsmore, R. H., Liberson, W. T., Henry, Pepe, A. Observations on Medical Temporal Lobotomy and Uncotomy in the Treatment of Psychotic States. *Proc. ARN & MD*, 1953.

Scoville, W. B. Orbital Undercutting in the Treatment of Psychoneuroses, Depressions and Senile Emotional States. *Dis. N. Syst.* Vol. XV, No. 11, 1954.

Scoville, W. B. and Ryan, V. G. Orbital Undercutting in the Aged. *Geriatrics*, Vol. 10, 311-317, July 1955.

Scoville, W. B. Late Results of Orbital Undercutting: Report of 76 Patients Undergoing Quantitative Selective Lobotomies. *Am. J. Psych.* 117, No. 6, Dec. 1960.

Some Observations Concerning Reading Retardation and Delinquency

T. P. Millar, M.D.

Introduction

This paper will report some observations concerning reading retardation and delinquency which were made in the course of a survey of the case records of boys at the Connecticut Junior Republic.* It was felt that this population afforded an unique opportunity for investigation of reading retardation and it was hoped to delineate this opportunity with sufficient detail to allow the design of a more definitive investigation.

As is often the case when data collected for another purpose is researched, its validity is conditional, impaired by a number of factors. The data used here is so impaired. The reading evaluations, for example were not all derived from the same test instrument. Also, while the Durrell-Sullivan Tests were administered by the same examiner, such was not true of the Stanford Achievement Tests. The Wechsler Intelligence Scale for Children was administered by many different examiners in many different settings. Similarly, the clinical histories sometimes lacked information, that, in retrospect, one might like to have known. Allowing for such, the findings are presented as suggestive, as pointing directions, and perhaps establishing the parameters of a more accurate study not subject to the handicaps of retrospective investigations.

General Characteristics of the Population

The Connecticut Junior Republic is a residential treatment program for boys thirteen to sixteen years of age. Schooling is conducted in residence for all but a small number of the boys, who attend local schools. The boys have histories of behavioral problems in schools or community that have, in almost all cases, brought them to the attention of the courts. In so far as the institution is not fenced, its population does not include the most driven delinquents, but it does care for many boys with severe acting out problems. Runaway, car theft, truancy, are frequent among the presenting problems.

There were fifty-five boys in the sample surveyed. The ages of the boys ranged from twelve years, five

months, to sixteen years, seven months. The average age was fifteen years, on month, which was also the mean age. All but ten of the boys were in their fourteenth or fifteenth year.

The Reading Data

Of the fifty-five boys, forty-five had been given Stanford Achievement Tests, and the reading portion of this test was used as a measure of the child's reading retardation. Thirty-two boys had Durrell-Sullivan tests. In general, the Durrell-Sullivan test was administered by the Remedial Reading teacher when she felt some reading difficulty existed. Where the child had both tests, the Durrell-Sullivan was used, since it was felt to be a somewhat more reliable indicator of the degree of reading retardation present.

The chronological age of the child at the time of testing was converted to a grade norm, using appropriate tables, and the reading grade obtained from the test was then subtracted from this grade norm to give a reading retardation score. The boys were then grouped according to degree of reading retardation. The following results were obtained:

	READING SCORES			
Group I	1-2	Grades Accelerated	4 Boys	
Group II	0-1	" "	6 Boys	
Group III	0-1	" Retarded	6 Boys	
Group IV	1-2	" "	7 Boys	
Group V	2-3	" "	11 Boys	
Group VI	3-4	" "	4 Boys	
Group VII	4-5	" "	6 Boys	
Group VIII	5-6	" "	7 Boys	
Group IX	Over 6	" "	4 Boys	

If one uses the frequently quoted figures of two years retardation as a cut-off point in determining a serious degree of reading retardation, it is evident that thirty-two boys (58% of the population) demonstrate such a degree of handicap. This data suggests the existence of three overlapping groups of readers, a group of good readers, a group 2 to 3

* The Connecticut Junior Republic is a residential program located in Litchfield, Conn. The assistance and cooperation of the Director, the school, cottage, and secretarial staff of the institution is acknowledged as having been vital to the conduct of this study.

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years retarded for reading and a third group of boys with very retarded reading skills.

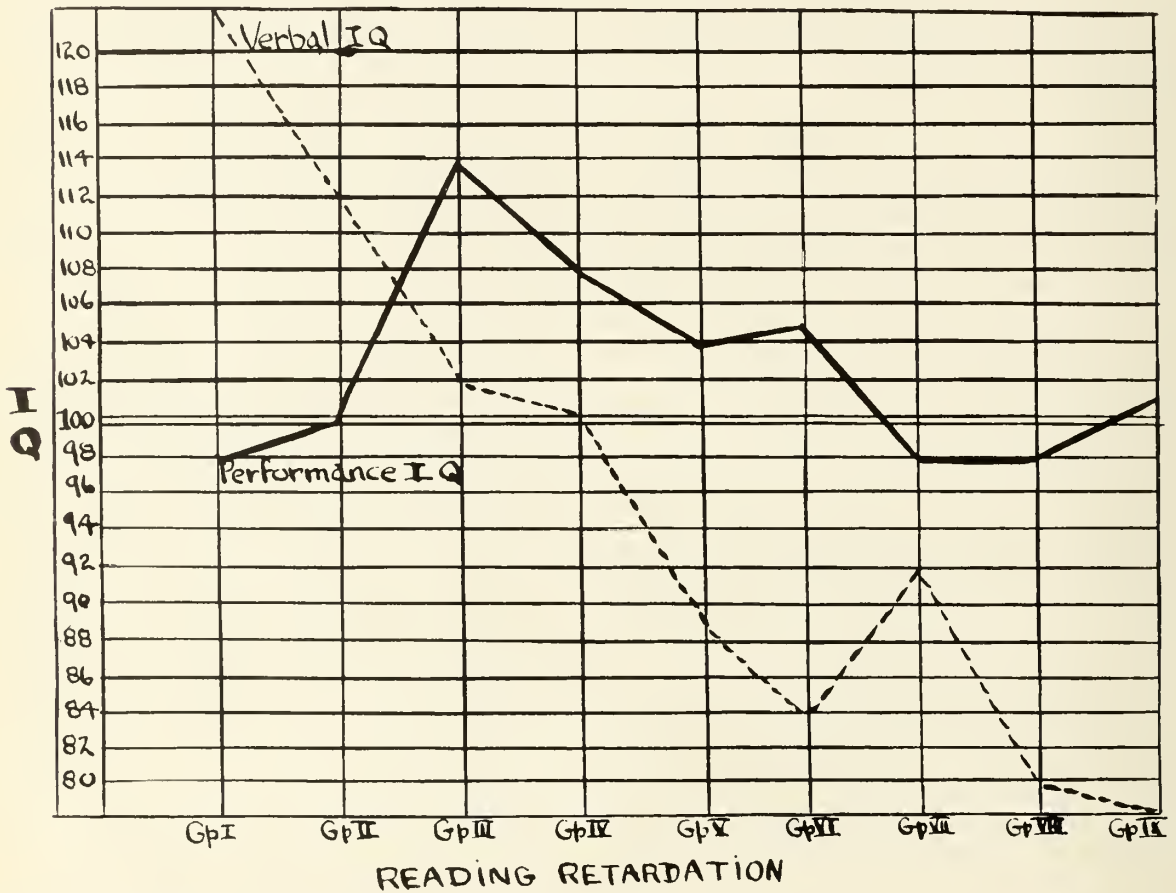
The Intelligence Data

Intelligence data was available on all fifty-five boys. Fifty-three boys had been given the Wechsler Intelligence Scale for Children, and of these, Verbal and Performance I.Q. figures were available on forty-eight. On one child, a Stanford-Binet I.Q. was available, and on another, an Otis.

All of the boys fell within the Normal ranges of I.Q., although Verbal-Performance discrepancies in both directions were marked, and occasionally one or the other score fell into Retarded ranges.

A relationship between reading retardation and Verbal I.Q. was noted, and is perhaps best illustrated by the following graph. The I.Q. Figures plotted are the average for the boys falling within the group with that degree of reading retardation:

RELATIONSHIP BETWEEN READING RETARDATION AND I.Q.



Examining this graph it is evident that with minor variations Verbal I.Q. tends to fall as reading retardation increases while performance I.Q. is maintained. A discrepancy between verbal and performance I.Q. develops and increases in magnitude as the degree of reading retardation increases.

Taking a closer look at the relationship between verbal-performance discrepancy and reading retardation the following was observed:

Top Ten Readers:

- 8 had over 10 pt. positive V/P discrepancies.
- 1 had an 18 pt. negative V/P discrepancy.
- 1 Unknown.
- Average V/P discrepancy was plus 15 pts.

Bottom Ten Readers:

- 6 had over 10 pt. negative V/P discrepancies.
- 2 had insignificant negative V/P discrepancies.
- 2 Unknown.
- Average V/P discrepancy was minus 19 pts.

Boys with Large Positive V/P Discrepancies:
(Over 20 and as high as 34 pts.)

There were 5 boys in which Verbal I.Q. exceeded Performance by over 20 pts. None of these boys was a significantly impaired reader and their average reading grade was 0.8 grades accelerated. In some cases, a low Performance I.Q. contributed to this discrepancy.

Boys with Large Negative V/P discrepancies:
(Over 20 and as high as 40 pts.)

There were 8 boys in whom Performance I.Q. exceeded Verbal by 20 pts. or more. All of these boys were over 2 grades retarded. Their average retardation was 4.9 grades—so they were not *all* the most severely retarded readers.

The data demonstrates that good reading ability is usually associated in this population with high Verbal I.Q., and poor reading ability is associated with low Verbal I.Q. Verbal-Performance discrepancy, however, does not seem to be so simply related to reading ability. Performance I.Q. tended to be higher than normal in many boys. For some of the very good readers, quite low Performance I.Q. contributed to the large discrepancies observed. Finally, quite high negative Verbal-Performance discrepancies were seen in some moderately retarded readers.

Wechsler²⁴ and Anastasi¹ report differences in Verbal-Performance I.Q. in relationship to nationality, cultural background, and delinquency, but what precisely is being measured here remains somewhat obscure.

Manipulation of Data

It is evident that to determine the grade norm expectancy of a child, solely on the basis of his chronological age, is to neglect differences in intellectual endowment, i.e., if a boy of fifteen be expected to function at a grade norm of 9.7, but his intelligence be deficient by 20 points from the normal 100, then it would seem appropriate to diminish the grade norm expectancy by 20%—that is, in this case, to a grade expectancy of 7.8. If by reading test a score of 7.8 were obtained without such a correction the boy would be considered to be 1.9 grades retarded. There would seem to be some point, therefore, in studies of reading retardation, in trying to adjust the expectancy of function to the child's intellectual endowment.

It is evident, however, that insofar as the Verbal I.Q. of the disabled reader reflects his disability (and also affects the Full Scale I.Q. on the WISC), that a valid measure of the disabled reader's intellectual endowment is not a simple matter to obtain. It has been suggested that the Performance

I.Q. represents a truer statement of the disabled reader's intellectual endowment.¹⁸

The following manipulation of this data was, therefore, undertaken. The grade norm of the child was adjusted via the following formula:

$$\frac{\text{Performance I.Q.}}{100} \times \text{Chronological grade norm} = \text{Adjusted Grade Norm.}$$

The reading grade obtained from the testing was then compared to the adjusted grade norm in order to arrive at an adjusted measure of reading retardation. This had some interesting effects. Specifically, this had the effect of shifting seven boys upwards, that is, to a less retarded reading category—and of shifting eleven boys to a worse degree of retardation. Of this latter, three boys were moved down two full categories in this table.

The boys who shifted upwards were boys with intellectual limitations, both Verbal and Performance I.Q. being below 100 and with insignificant discrepancies in all but two cases. It would seem that for children with limited endowment, correcting for intellectual endowment does produce a more realistic measure of reading retardation.

The eleven boys whose retardation score was made worse by the correction had, in all but one case, significant Verbal-Performance discrepancies, in favor of Performance I.Q. The potential of these boys, as measured by their Performance I.Q., was higher than their age expectancy and resulted in a highlighting of their reading handicap. In most cases, these seemed to be truly disabled readers.

There were thirty boys whose standing was not significantly altered by this manipulation of the data. Also there were, as mentioned previously, seven boys to whom this procedure could not be applied, due to the lack of Verbal-Performance I.Q. data.

Discussion

It is evident that significant reading retardation is common among the delinquent population examined. It seems probable, in terms of capacity for language function, that more than one group or class of boys is represented in this population. Three groups suggest themselves:

(1) There is clearly a group of competent readers. These are children, however, whose social adjustment has been such as to bring them to a residential facility for acting out boys. This group is atypical and interesting.

(2) There is a group of poor readers, sometimes very significantly disabled for reading, whose in-

telligence, particularly as measured by Performance I.Q., is Normal or Superior. Such boys frequently demonstrate fairly large Verbal-Performance discrepancies. The author examined two of these boys and found conceptual inadequacies such as Rabinovitch describes in relation to primary reading disabilities to be present.¹⁸ One wonders if such might not have been found more commonly in boys with large negative Verbal-Performance discrepancies, normal intelligence, and marked disability for language function.

(3) There is also a group of poorly reading boys with Normal or Dull-Normal I.Q. and little discrepancy between Verbal and Performance I.Q. scores. Their disability for language is often not so marked as the former group.

To discriminate these groups from one another, and perhaps to uncover other groups, will require an investigative design that will make explicit the varying cognitive capacities and styles, as well as the delinquent patterns, life experiences, and personality traits of the boys. Such is clearly beyond the scope of this survey.

In the course of reviewing the clinical histories of the boys, certain differences between the delinquent boy who reads well and the delinquent boy who reads poorly become evident. Again, in the hope of bracketing those areas where further investigation seemed warranted, the author reviewed the clinical histories of the top ten reading boys, and compared these with the clinical histories of the ten boys with the worst reading scores. While the groups were not completely homogenous, a good deal of similarity was noted within each. The differences of these groups one from another were striking, and it is felt that this qualitative data is most usefully reported in terms of those differences.

Good Readers—Poor Readers, Contrasted

One of the areas of notable contrast was in the behavioral patterns of the boys as this was reflected in the symptoms that led to their commitment to the institution and in their behavior within the institution.

The good readers were considerably more explosively impulsive, more driven in their behavior. Defiant, rebellious behavior in school or community, runaway, car theft, vandalism, and sometimes assaultive behavior characterized their delinquent histories, which tended to be of shorter duration than the poor reading group. In the institution, these boys were troublesome, disruptive, and problems in management. They were abrasive, provoca-

tive, active boys capable of relating meaningfully to staff and the other boys, but frequently doing so in hostile, disjunctive ways. While it is rare for boys to be discharged from the Connecticut Junior Republic administratively—that is, because they cannot be managed in the program, several of this good reading group had been so discharged, while none of the poor reading group had left via this route.

The poor readers' contact with the Juvenile Court had frequently led to their being adjudged Neglected, rather than Delinquent. While delinquent behavior is frequent in the histories of these boys, it does not have the impulsive and explosive character noted above. Symptoms tend to be chronic and to involve such things as poor achievement in school, chronic truancy, enuresis, stealing, disobedient behavior, and poor peer relationships in school. Their histories are punctuated with occasional episodes of aggressive, hostile behavior. Five of these ten boys had residential treatment prior to coming to The Connecticut Junior Republic for periods ranging up to three years. In the institution, these boys were passive peripheral boys, rarely management problem. They tended to relate minimally with much less emotional investment and a good deal less interpersonal turmoil.

The circumstances of the boys' rearing, their family backgrounds, were strikingly different. The poor readers came from chaotic, disrupted families. Breaks in the continuity of their reading were very common. One or the other of their disturbed parents had deserted, been jailed or hospitalized, at one time or another. Multiple marriages, foster care, brief periods of care outside of their homes, were common. The fathers were unknown—at least to the child—in three cases, were dead in two other cases, and were jailed in another two cases. These men were frequently inadequate or antisocial individuals with poor employment histories. They brought little strength to their families, but, instead, introduced disruption in the form of alcoholism, incest, or brutality. The mothers were also very disturbed persons. Illegitimacies, multiple marriages, desertions, testified to their social incompetence. These women were unable to control their sons, and frequently sought to be relieved of the responsibility. It was just such chaotic home situations that had frequently led to the placement of their children outside of the home. It can be said that the home life of these boys had been such as to deprive them of the most elemental emotional

gratifications, as well as to offer them almost no consistent socializing experience.*

The family patterns of the good reading group were distorting environments also, but not the grossly depriving situations described above. Over half of these homes were intact, and those that were broken tended to be more recently so—and in two cases, by death. Breaks in the continuity of the child-reading environment were much less common. The mothers had not been involved in multiple marriages in most cases, nor illegitimacy or desertion. They tended to be over-involved with their sons in ways that interfered with the mother's ability to set limits and which appeared in many cases to be stimulating to the boy involved. The fathers, while they had provided for their families, tended to be ineffectual, psychologically absent, and not infrequently the object of their sons' contempt. There were not, however, the severely disordered individuals seen in the poor reading group.

The quality of the homelife of these children might be characterized as more distorting than depriving—at least, when one contrasts it with the poor reading group.

One thing emerged quite clearly, and that is that the good reading delinquent is atypical, at least in this institution. There was frequently some aspect of him that was unusual. One boy was a private case; that is, he was the only boy in the program whose care was not paid for by the State—his well-to-do parents financed his institutionalization. Another boy had an endocrine disorder that had produced precocious sexual development and dwarfism. A third was a boy whose acute school refusal had ultimately led the Court to commit him.^{15, 16} Two boys' violent hostility to their mothers—in one case involving threats with a knife—led to their institutionalization. The clinical situation was, therefore, frequently unusual in some particular and important aspect.

In brief summary, then, it seems that the good reading delinquent tends to be impulsive, intensely conflicted, and unable to bind his distress. His delinquent acts seem to be triggered by events which intensify his conflicts, or perhaps overwhelm his limited capacity to bind affects and control his behavior. His life situation is a distorting one, more

characterized by troubled interpersonal relatedness than a lack of relationship. He is perhaps a neurotic delinquent.

The poor reading delinquent observed seems to be a more characterologically deviant child. His inner conflicts do not seem to have the same intensity; he does not, despite very severe deprivation, appear to be experiencing the driving turmoil of the good reading delinquent. His behavioral symptoms and delinquent acts tend to be chronic, more an integrated aspect of his personality, triggered more by opportunity or situational factors than increased inner tension. His home environment has deprived him of the basic necessities of psychological growth, leaving him dependent, mutilated, and with a limited interest in, or capacity for, human relationship.

Discussion

The high incidence of reading retardation amongst delinquent children has been noted for some time, but the relationship between these symptoms has remained unclear. Obviously, to be unable to read in a highly developed society is a serious handicap, one that will certainly interfere with successful adaptation and may press toward a delinquent life pattern. On the other hand, the rebellious antisocial orientation of the delinquent child clearly contributes to an intolerance for learning. Even so, it seems unlikely that either of these explanations is adequate to account for the complexities observed.

Delinquency is a symptom, one that appears in more than one constellation of psychopathology. Most observers recognize at least three such constellations:

(1) The emotionally disturbed or neurotic delinquent.

(2) The socialized or "normal" delinquent; normal only in the sense that his antisocial behavior is congruent with the values of his subculture.

(3) The unsocialized, aggressive delinquent, whose problems are pervasive and severe.

Similarly, reading retardation is a symptom appearing in more than one constellation of deficit. A child may be unable to read because his cognitive function has been impaired by organic factors. Also, we know that the emotionally disturbed child often reads and learns poorly, most frequently as a non-specific consequence of his emotional turmoil and adaptive immaturity. Finally there is the dyslexic child who has evident cognitive handicaps without evidence for organic origin.

* Three of ten homes in the poor reading group were intact, and while they were troubled environments, they had offered some continuity of care and less marked deprivation than the pattern described above. Interestingly, two of the boys involved had no significant Verbal-Performance discrepancy, while that of the third was unknown.

Due to the limitations of the data obtained in this study we are not able to apply either the categories of delinquency or of reading retardation to this population in any but a most impressionistic way. The data does suggest however, that the top ten readers described are emotionally disturbed delinquents, while the bottom ten readers belong to the category of unsocialized aggressive delinquent. If this be so, then severe reading disability may be more common in this latter class of delinquents.

Further, the quality of the reading retardation in this latter category of delinquents points toward a true cognitive deficit (rather than a practice deficiency) as the root of the learning problem. If this be so, and the idea certainly seem worth pursuing further, then one is led to wonder whether very severe deprivation such as these children experienced in their rearing years cannot interfere as drastically with cognitive maturation as it does with adaptive development. It is possible that dyslexia may sometimes be a sequela of a life situation that fails to offer the child opportunity for intellectual maturation.

It is also possible, at least for this group of children, that the relationship between reading retardation and delinquency is incidental rather than causal. Both may stem from a more basic defect. In a previous publication¹⁴ I have suggested that the cognitive handicap, the incapacity for language and symbol function, may not only interfere with learning to read, but also may limit the psychological defenses the child can mobilize to deal with his intense conflicts. Unable to dissipate his anxiety and hostility through words, and unable to contain or control it through symbolic defensive constructions, the child may have little alternative but to act out his distress and become delinquent.

Obviously, there is a pressing need for extensive study of these problems, and equally obviously, such study will have to be so designed as to take into account the many variables that complicate this picture. However, there are present educational realities that are even more pressing.

The classrooms of institutional schools are filled with boys for whom education has meant only frustration and failure. These boys have, in some cases, unknown cognitive impairments. They are, at this point, unmotivated for learning. They have, in many cases, experienced deprivation of their most elemental emotional needs. They have not found a way to relate to the society that has so deprived them. In this, the age of the explosion of

knowledge, of automation and anomie, they face a bleak prospect indeed.

In order to educate these children, it is first necessary to meet some of their emotional need. It is necessary also to contain them, to protect our society from them, and to do so in such a way as to lead these children back to a place in the fabric of community life. Finally, it is necessary to understand their cognitive incapacity, to learn how this was engendered, how the maturational process has been distorted or perhaps halted. If it is not too late, and the child's emotional needs can still be met, and he can be contained, perhaps it is possible to once again set the maturational process in motion.

Research is needed to understand these matters better. At this time the school must deal with these children in terms of its present understanding. It needs to encourage experimental approaches, such as that of Kephart in his perceptual re-training.¹² The school must adjust its expectations to present abilities and problems of the child. The hierarchy of educational tasks such as outlined by Hewett is an interesting example of such modification of expectations.¹⁰ This hierarchy of tasks has the virtue of not losing sight of the instructional goals of the school.

It should be recognized that institutional schools are not regular classroom situations. These are almost entirely re-educational or remedial situations. The staff expectancies and the budget of the institutional school must respect this reality.

Until such times as remedial techniques, based upon a comprehension of the cognitive deficits of the children, are developed, education of these children will remain a holding operation. The social consequences of this are, as pointed out in the McCone report, *Violence in the City*, potentially devastating. Vigorous research activities in this area are mandatory.

Summary

This paper reports upon a survey of reading abilities and aspects of intelligence amongst a group of delinquent boys. The good reading delinquent boys are contrasted with the poor reading delinquent boys, and some striking differences are observed. The associated educational realities are explored.

Bibliography

1. Anastasi, Anne; *Psychological Testing*: The McMillan Company, New York, 1961. Page 318.

2. Belmont, L. and Birch, H. G.: *Lateral Dominance and Right-Left Awareness in Normal Children*; Child Development, 1963. Vol. 34, Pages 257-270.
3. Birch, H. G. and Belmont L.: *Auditory Visual Integration in Normal and Retarded Readers*; American Journal of Orthopsychiatry; Vol. 34, No. 5, October, 1964.
4. Birch, H. G.; *Dyslexia and the Maturation of Visual Function*, In Money, Reading Disability; Johns Hopkins Press, Baltimore, Md., 1962.
5. Braun, J. S.; *Relationship Between Concept Formation Ability and Reading Achievement at Three Developmental Levels*; Child Development, 1963. Vol. 34, Pages 675-682.
6. Deutch, M.: *The Role of Social Class in Language Development and Cognition*; American Journal of Orthopsychiatry; Vol. 35. No. 1, January, 1965.
7. Flavell, J. H.: *The Developmental Psychology of Jean Piaget*; D. Van Nostrand Co., Princeton, New Jersey, 1963.
8. Friedman, F., Golomb, J. and Mora M.: *The Hair Whorl Sign for Handedness*; Diseases of the Nervous System; Vol. 13, 1952. Pages 208-216.
9. Fuller, G. B.; *Perceptual Considerations in Children with a Reading Disability*; Psychology in the Schools, Vol. 1, No. 3, Pages 314-317, July, 1964.
10. Hewett, F. M.: *A Hierarchy of Educational Tasks for Children with Learning Disorders*; Exceptional Children; Vol. 31, No. 4, December, 1964.
11. Kawi, A. A. and Passamanick, B.: *Association of Factors of Pregnancy with Reading Disorders of Childhood*; Journal of American Medical Association; Vol. 166, March, 1958.
12. Kephart, N. C.: *Perceptual Motor Aspects of Learning Disabilities*; Exceptional Child; Vol. 31, No. 4, December, 1964.
13. McCone, et al; *Violence in the City, An End or a Beginning*, as quoted in Social Service Review, Vol. ..., March, 1966. Page 87.
14. Millar, T. P.: *Reading Retardation*; Northwest Medicine, November, 1960.
15. Millar, T. P., Radman, R. J., Sneed, D.: *Program Development in a School for Delinquent Boys*; Social Casework, November 1960.
16. Millar, T. P.: *The Child Who Refuses to Attend School*; American Journal of Psychiatry, Vol. 118, No. 5, Nov. 1961.
17. Money, J.: *Reading Disability; Progress and Research Needs in Dyslexia*; Johns Hopkins Press, Baltimore, Md., 1962.
18. Rabinovitch, R. D., et al; *Research Approach to Reading Retardation*; Association for Research in Nervous and Mental Disease Processes; No. 34, Pages 363-396. 1954.
19. Rabinovitch, R. D.; in Money; *Reading Disability*; Johns Hopkins Press, Baltimore, Md., 1962.
20. Shaw, C. R. and Fuller, G. B.; *Visual Orientation in Reading Disability*; Journal of American Academy of Child Psychiatry; Vol. 2, No. 3, July, 1963.
21. Switzer, J.; *A Genetic Approach to the Understanding of Learning Problems*; Journal of American Academy of Child Psychiatry. Oct. 1963.
22. Tien, H. C.; *Use of the Organic Integrity Test with Children Who Can't Read*; American Journal of Psychiatry; Vol. 22, No. 10. 1966.
23. Tjossem, T. D., Hansen, T. J., Ripley, H. S.; *An Investigation of Reading Difficulty in Young Children*; American Journal of Psychiatry; Vol. 118, No. 12, June, 1962.
24. Wechsler, David; *Measurement of Adult Intelligence*; Williams and Wilkins Press, 3rd Edition. 1944.

Bygones and Expectations

Any retrospect . . . of the [surgical] work of the decade furnishes good warrant for pride in what has been, and high hopes of what is to be. The world over, educated minds and trained hands are busy with the problems of cause, of course, of termination, and seeking out surer, safer, and speedier means of relief, therapeutic and operative. Week by week, and month by month, what is accomplished becomes free and common property; everything is proven, and the good held fast. What will be the outcome of all this thinking, and experimenting, and operating, and writing, even in the near future, who would dare to predict? American surgeons have had not a little to do with the work in the past. Fellows of our [American Surgical] Association, some of whom have fallen asleep, have been closely identified with the discovery, the early adoption, and the thorough testing of not a few methods of treatment, and we may expect with confidence that it will be with us hereafter as it has been, and yet more.—Conner, P. S.: Address of the President, American Surgical Association, *JAMA* 18:758 (June 11) 1892.

Utilizing Health Personnel In Extension's Education Program

G. S. Gudernatch, M.D.

In recent years, the Cooperative Extension Service has been concerned with an increasing range of community problems. A number of changes and revisions have been made in Extension's organizational structure at local levels in attempts to explore these problems in greater depth. Program planning groups such as Extension Advisory Committees, County or Rural Area Development Committees, and/or County Extension Councils (both youth and adult) have been established to assist with overall planning on broad and significant problems. These committees are organized country-wide and represent a cross section of community interests. As fact finding bodies they can well serve as nuclei for health planning.

A committee representing volunteer and official health agencies, the medical and nursing professions, hospitals and nursing homes, and other health facilities such as rescue and transportation squads as well as community leaders, can give leadership and guidance in planning for the development or reorganization of health services. These leaders must inform themselves of the needs to make sound decisions. Health planning is an important part of a community's total development plan. The ramifications and complexity of health problems today require a multidisciplinary approach, utilizing the resources of a multiplicity of agencies.

A main function of Extension workers is to effect social change. At the county level they can begin now to lay some of the groundwork for community planning in the development of health services. They may:

1. Visit local health and welfare agencies to find out about their services and programs.

DR. G. S. GUDERNATCH, Active Staff and past Chief of Staff at Sharon Hospital; member of the courtesy staff of the Wassaic State School Hospital, Wassaic, New York. "Member, AMA Council on Rural Health".

Presented at the Seminar for Extension Specialists in Health Education and Related Fields sponsored by the AMA Council on Rural Health, Philadelphia, Pennsylvania, March 20, 1969.

2. Establish a system of communication on a permanent and continuing basis to coordinate education efforts and strengthen working relationships among all agencies concerned with improving health.

3. Explore informally the health service problems with community leaders and professional health workers.

4. Organize a health committee as part of the Extension Community Development Committee which may serve as a nucleus for a community-wide fact finding and health planning body.

5. Interpret the functions of the health committee to local medical, education, public health, welfare, voluntary health, and other groups and agencies in a position to give professional leadership.

6. Help people gain an awareness of the need for community-wide planning for adequate and comprehensive health services.

7. Encourage an interest in conducting a self-study and developing community readiness with the professional leaders of a community.

8. Make an inventory of the existing health agencies, services, and programs available to a community.

9. Gather and collate the points of view of rural people about their existing health needs and resources, and transmit these back to the health professions and agencies for their use in providing the best educational programs and services to the community.

Doctors of medicine educate patients about their physical and emotional problems and how to cope with them. Physicians find themselves searching for words and methods of explanation for their patients' needs. The physician specializes with a patient, then he generalizes, but most important, he individualizes his teaching to the apparent need and comprehension of his patient. He is more than a healer. He IS a teacher, this fact a physician cannot forget. Some of us are better at teaching our

patients than others. More understanding about health education as a process would help the physician fill this role better with his patients and his community.

A multiplicity of services and resources is offered by State Departments of Health and Cooperative Extension Services. Both agencies have some basic philosophies, methods, and techniques in common, and work with people to help them meet their needs. No single organization can do the job alone. So, we use all the resources at hand to develop the best program possible.

Webster defines resource as "a reserve source of supply or support, or skill in meeting a situation". A good working relationship between health departments and Extension Services is necessary for an improved community health. There must be a give and take feeling between them; they must help and support each other; and they must communicate with each other if their resources are to be utilized most effectively.

Also a decreasing number of professional health workers, particularly physicians, but others as well, means that rural people have to face up to changes in the methods of delivering health care. Extension Service workers who provide guidance in health education programs need to inform themselves of new developments. Electronics will play a greater role in rural health. Experiments in the use of television in diagnosis and treatment suggest interesting, albeit still remote possibilities.

Rural people will need more positive health teaching to give them a better basis for improved health practices. More and more of this education will need to be done by persons other than physicians or by physicians at a greater distance. In Boston, we have a Medical Reports TV program, originally directed at rural physicians in Maine, but now reaching a wider audience. Video tapes are shared by them with other parts of the nation, and films are used for teaching programs with hospital staffs and local physicians. We had a regional rural health conference on nutrition in Vermont a few years ago which was similarly taped and televised.

Why could this method not be adapted to get high quality health education programs to the public? If, for instance, a community is doing a good job in one particular program, it could be recorded and made available for use elsewhere. Such productive use of the talents of skilled professional personnel should provide effective teaching to the public. The Extension worker could alert and prepare communities for the use of such a program.

It would reduce unreasonable demands on the time of physicians and other health professionals where they are not easily available for educational activities.

Health programs are an integral part of 4-H work. These young people can be taught the best in nutrition, hygiene, accident prevention, etc. Yet apathy or lack of enthusiasm on the part of both youth and adults for the need for programs in health, safety and first aid often provide a stumbling block in their presentation. A lack of qualified resource people causes a hiatus in the experienced direction so necessary for young people. Health workers must provide these necessary resources. The health aspects of all 4-H projects should be an integral part of the 4-H program.

Over 80% of our state medical associations have active committees on rural health and a rural health chairman of the woman's auxiliary to the state medical association. Their work forms the basis for effective coordination and implementation of programs at the state and local levels designed to improve the health of people living in rural communities. In addition, several states and regions have health councils whose programs encompass rural health needs. The State Extension staff should establish effective communication channels with the state medical association and in turn the rural health committee of the state association.

Finally physicians and health workers have long recognized the need for community health planning to prevent fragmentation of services, needless duplication of these services and a waste of money and resources, not to mention the need for conservation of human energies of physicians, nurses, dentists, public health, and other health workers. Local physicians are generally glad to help with educational programs when given the opportunity. Since health is a community affair, it includes all those who work together to improve the health of the people.

I should like particularly to congratulate the Extension Services for the effective health education programs they have conducted in the past, and to commend them for their present endeavors and their plans for the future. In many states, tremendous strides in health education have been made because of the initiative and perseverance of many people in Extension. The health education specialist can be the catalyst or the real force to bring the rural population in closer contact with the health services providers and to raise the standards of rural health.

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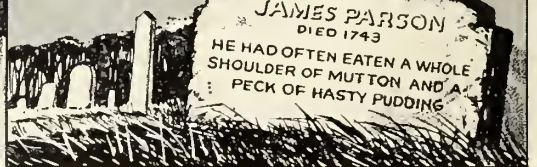
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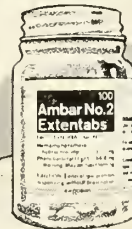
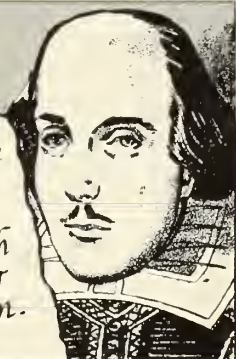


JAMES PARSON
DIED 1743
HE HAD OFTEN EATEN A WHOLE
SHOULDER OF MUTTON AND A
PECK OF HASTY PUDDING

SHAKESPEARE

WAS AWARE OF THE
DANGERS OF OBESITY
HE WROTE...

*Make less thy body hence
and more thy grace,
leave gormandizing;
Know thy grave doth
gape for thee wider
than for other men.*



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BRIEF SUMMARY/Indications: Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

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THE PRESIDENT'S PAGE

Confrontation and challenge are the bywords of this generation. Students are testing the establishment. The races are confronting one another. Law and order is being challenged from all sides. The consumer is balking at prices and taxes. Forces of all kinds—political, social, economic—are trying to shape events to their idea of milieu.

The medical profession, too, has been handed a challenge by these forces. That challenge, as I see it, is not to resist change—the evolution of high quality medical care, medical education, and other desirable health practices under the direction of organized medicine attests to that fact. No, the challenge is to resist unwise and unwarranted government control of our profession and to preserve and to strengthen the time-tested medical practices which have made the health care available to Americans the best in the world.

One might ask, what is it that has made the delivery of health care in Connecticut second to none? It is the freedom of the physician to operate within the free enterprise system for the good of the patient; to develop a private patient-physician relationship with its manifest benefits to the patient, to encourage free choice of physician by the patient so that the patient may select the level and continuity of care he feels is best for him; and, finally, to assure medical care to the indigent on the same footing as all others.

It is clear by the drift of medical legislation in recent years that this desirable system is being seriously threatened. Government has entered the health care field with foreboding portents for medicine—foreboding because government has a dismal record of managing its affairs.

In an editorial some time ago the Norwich Bulletin declared that the federal government “is unable to institute any kind of cost control in its operations, any sort of modernization in most of its procedures, and many of its basic services, such as the postal service, have come close to collapse.

“With such demonstrated management incapacity, it is inconceivable anyone would suggest the government should take over responsibility for more of the management of the country's affairs. Yet, this is happening and in the critical field of medicine.”

Unwise labor policies are placing the yoke of high costs around the neck of the entire health profession. And various uninformed individuals would tamper with the practice of medicine—in offices, in hospitals, in clinic—for political gain or in pursuit of “ideological” goals.

As physicians we are committed, as always, to the health and well-being of our patients. It is our duty to resist the forces which would regiment us and thereby weaken our ability to provide the best medical care possible. Let us all meet these challenges head on.

STEVENS J. MARTIN, M.D.

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Josephine P. Lindquist
Associate Executive Director

SUMMARY OF ACTIONS COUNCIL MEETING Wednesday, June 4, 1969

I. Attendance

Present were: Drs. Martin, Granoff, Weber, Jr., Edson, Brandon, Abbot, Dean, Gardner, Fabro, Polivy, Rogol, Cramer, Harwood, Petrie, Wilson, Jr., Purnell, Grant, Nemoitin, Roch, Johnson, Pelz and vonGlahn.

Also present were: Mrs. Lindquist, Mr. Villano, Dr. Friedman (President, FCMA), Dr. Nolan (Vice-President, FCMA), Dr. Patterson (Dean, UConn Medical School), Dr. Hess (Medical Director, State Welfare Dept.) and Dr. Richards.

Absent were: Drs. Farrell, Friedberg, McDonald, Palomba and Klare.

II. Organization

The meeting was called to order by the President, Dr. Stevens J. Martin, who introduced the guests present, the new CSMS officers and the County Association Councilors and Associate Councilors. He then declared the floor open for nominations for the office of Chairman of the Council for 1969-70. After several nominations and declinings thereof, it was VOTED to elect Dr. Martin to the chairmanship by acclamation. Following his remarks of thanks and acceptance, Dr. Martin declared the regular meeting of the Council to be in session.

III. Routine Business

Life Memberships

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

Angelo L. Gentile, New Haven (NHCMA)—1969
Russell A. Keddy, Stamford (FCMA)—1969
Hyman A. Levin, New Haven (NHCMA)—1969
Ludwig L. Markley, Bridgeport (FCMA)—1969
F. Brae Rafferty, Chaplin (WCMA)—1969
Robert Tennant, West Hartford (HCMA)—1970

CSMS Dues Exemptions

It was VOTED to exempt from payment of CSMS membership dues the following Active Members for the indications and periods stipulated:

Ralph W. Haswell, Sudbury, Mass. (MCMA)—1969—Physical Disability

Sidney Hurwitz, New Haven (NHCMA)—1969—Postgraduate Education

Martin J. Kligerman, West Haven (NHCMA)—1969—Postgraduate Education

Brendan E. Melvin, Framingham, Mass. (TCMA)—1969—Postgraduate Education

Committee Resignations and Appointments

(a) *Committee on State Blood Bank*: It was VOTED to accept the resignation of Nelson A. Gelfman, Danbury, as a member of this Committee. It was further VOTED to appoint Peter W. Pratt, Danbury, to membership on the Committee for 1969-1970.

(b) *Advisory Committee to State Board of Examiners for Nursing*: It was VOTED to accept the resignation of Frederick W. Goodrich, Jr., New London, from membership of this Committee. It was further VOTED to appoint Reginald C. Edson, West Hartford, to replace Dr. Goodrich as a member of the Committee for 1969-1970.

(c) *Committee on Medicine and Religion*: It was VOTED to accept, with regret and thanks for past service, the resignation of Francis W. Helfrick, Manchester, as chairman of this Committee. It was brought to the Council's attention that Joseph C. McCarthy, Torrington, has left the state permanently and it was therefore VOTED to delete his name from the Committee roster. It was further VOTED to reconstitute the Committee for 1969-70 as follows:

Joseph J. Kristan, Rockville, Chairman
Francis W. Helfrick, Manchester
Samuel Climo, New Haven
Eugene H. Corley, Bridgeport
E. Marvin Henken, Hartford
Nicholas T. Phillips, Norwich
James P. Roach, Bridgeport
Louis Rogol, Danbury

(d) *Committee on Occupational Health*: It was VOTED to accept the resignations of Harold Schwartz, Hartford, and Charles Sheard, Stamford, as members of this Committee.



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Gantanol[®]

(sulfamethoxazole)

for the pathogens

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Indications: Urinary tract infections with associated pain or discomfort when due to susceptible organisms; prophylactically in urologic surgery, catheterization and instrumentation.

Contraindicated in sulfonamide-sensitive patients, pregnant females at term, premature infants, newborn infants during the first three months of life, glomerular nephritis, severe hepatitis, uremia and pyelonephritis of pregnancy with gastrointestinal disturbances.

Warnings: Use only after critical appraisal in patients with liver damage, renal damage, urinary obstruction or blood dyscrasias. If toxic or hypersensitivity reactions or blood dyscrasias occur, discontinue therapy. In closely intermittent or prolonged therapy, blood counts and liver and kidney function tests should be performed.

Precautions: Observe usual sulfonamide therapy precautions including maintenance of an adequate fluid intake. Use with caution in patients with histories of allergies and/or asthma. Patients with impaired renal function should be followed closely since renal impairment may cause excessive drug accumulation. Occasional failures may occur due to resistant microorganisms. Not effective in virus and rickettsial infections.

Adverse Reactions: Headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, Stevens-Johnson syndrome, injection of the conjunctiva and sclera, petechiae, purpura, hematuria or crystalluria may occur, in which case the dosage should be decreased or the drug withdrawn.

Dosage: Adults—4 tablets initially, then 2 tablets morning and evening.

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(c) *Committee on Rehabilitation*: It was VOTED to appoint new members to this Committee for 1969-70 as follows:

James E. C. Walker, Hartford
John J. Lawrence, Bridgeport

Date of Next Meeting

The Chairman announced that he planned not to call a meeting of the Council during the month of July, unless it becomes necessary, and to schedule the next meeting for Thursday, August 14, 1969 (tentatively).

IV. Old, New and Special Business

Review and Reappointment of Council Committees, Subcommittees, Etc.

All standing committees and subcommittees of the Council, as well as special (ad hoc) and advisory committees appointed by the Council, were reviewed. Where appropriate, replacement and/or addition of members was made. In several instances, committees were discharged for the reason that they had fulfilled their assignments and were no longer active or needed.

Discharged were:

Advisory Committee on Recognition for CSMS Service

Ad Hoc Committee to Study CRMP Organization and Structure

Ad Hoc Committee to Study Feasibility of CSMS Fee Survey

Ad Hoc Committee to Develop Alternative Legislative Proposal for Medicaid

Advisory Committee on Cardiovascular Diseases

Representatives to Connecticut Mental Retardation Planning Project

Advisory Committee to Public Health Nursing Section (State Dept. of Health)

Advisory Committee to Conn. State Bureau of Rehabilitation and Disability Determination Unit, Connecticut State Department of Education

Representatives, State Operational Survival Plan

Advisory Committee to State Workmen's Compensation Commissioners

Change of name and assignment:

Ad Hoc Committee on Liaison with Chiropractors to Ad Hoc Committee to Study Problems of Osteopathy

Report—2nd AMA National Conference on Nursing

It was VOTED to accept, with commendation, a report on the proceedings of this Conference

(Chicago, April 11-12) filed by Hilliard Spitz, New London, who attended as a representative of the Society. It was further VOTED to approve four recommendations which accompanied the report, three in full and one with a partial contingency. In brief, the recommendations called for the planning and holding of a first "Connecticut Conference on Physician-Nurse Relationships" in the late Fall of 1969, with Dr. Spitz to serve as chairman of a committee on arrangements. Joint sponsorship of the Conference would be sought from the Connecticut Nurses' Association and the Connecticut League for Nursing. The partial, contingent approval was given to a recommendation that the Council give prior approval to a blanket fixed sum in contribution to cover the expenses of the Conference. On this point, the Council expressed favor for authorizing the expenditure of any reasonable amount, up to a total of not more than 60% of complete costs of the Conference, in consideration of the contributions made by other co-sponsoring agencies. However, the Council will request that Dr. Spitz submit a detailed budget in order that the CSMS contribution can be assessed more accurately, and that if the CSMS contribution is expected to exceed the 60% level of total anticipated costs, Council approval of the overage must be sought in advance.

Report—65th Annual Congress on Medical Education

It was VOTED to accept, with commendation, a report on the proceeding of this Congress (Chicago, 2/69) filed by C. Louis Fincke, Stamford, who attended as a representative of the Society. It was further VOTED to send copies of Dr. Fincke's report to the members of the Committee on Postgraduate Education as information.

Report—Committee on Allied Medical Services

The Committee brought to the Council's attention the fact that many of the state's community colleges are developing certification programs for various types of technologists in the field of medicine, and that the State Department of Education's Committee on Higher Education is desirous of having a panel of physicians to advise on the professional aspects of these educational programs for technologists. It was VOTED to accept the Committee's report and approve its recommendation that the Society form such a panel of professional advisors and make same available, on request, to the Committee on Higher Education. It was further VOTED that the selection of panel members for this purpose be made from two sources: (a) the

Committee on Allied Medical Services, and (b) the County Medical Association Councilors and Associate Councilors. In addition to Dr. Spitz and his Committee, the County Councilors and Dr. James of the Committee on Higher Education, Commissioner Foote of the State Health Department is to be informed of these actions.

Connecticut Regional Medical Program

Having received a request from CRMP to make nominations for service with CRMP Technical Advisory Committees to three projects being implemented (CUPISS, Coronary Care Training Program and Regional Medical Library Service Program), it was VOTED to ask the Chairman to appoint an ad hoc committee to select and make recommendations to the Council concerning qualified nominees for these assignments (at least two nominees for each TAC; preferably more than two). The Chairman appointed the Ad Hoc Committee on CRMP Technical Advisory Committee Nominations as follows:

- Morris A. Granoff, New Haven, Chairman
- Michael A. Dean, Bridgeport
- Clifford E. Wilson, Jr., Norwich
- Leo P. Giardi, Hartford

It was VOTED to accept as information verbal reports presented by Drs. Abbot, Johnson and Martin (CSMS designates serving on the CRMP Advisory Board) concerning recent developments in CRMP with respect to greater physician representation on the CRMP Advisory Board and Executive Committee. In brief, the collective sense of these reports was that most of the other members of the Advisory Board were *not* disposed to increase the number of practicing physician representatives at this time and were, in fact, moderately to markedly opposed to any such increase.

Resolution—Membership in CSMS Sections

It was VOTED to receive as information a resolution submitted by the Executive Committee of the Section on Orthopedics which informed the Council that many new members of the Society are not joining this (and probably other) Section and appear not to be aware that the Section exists. Pursuant to the receipt of this information, it was further VOTED to publish an article in the Journal which describes the structure and functions of Sections and the manner in which new members should go about applying for Section membership. Reprints of this article will then be included in the “membership kit” which all new CSMS members receive upon election.

COMPAC

- (a) It was VOTED to receive as information, and with thanks, notice from Francis Gallo, COMPAC Board Chairman, that he had appointed an ad hoc committee to review COMPAC’s experience in political education and action since its formation in 1962 and transmit a report of its findings to the Council at an early date.
- (b) Since the House of Delegates had referred back to the Council for further study the Council’s report and recommendations concerning proposed changes in CSMS-COMPAC relations, particularly with regard to certain legal questions that CSMS counsel has raised, it was VOTED to reappoint an Ad Hoc Committee on CSMS-COMPAC Relations to make this further study, as follows:

- Morris A. Granoff, New Haven, Chairman
- Sidney L. Cramer, Hartford
- Clifford E. Wilson, Jr., Norwich

**Report—Efforts to Restore
“Usual and Customary” to Medicaid**

It was VOTED to receive as information verbal reports presented by Drs. Martin, Polivy, Cramer, Hess and Richards on the efforts that have been made to get a bill passed which would authorize the resumption of the “usual, customary and reasonable charge” method of payment for physicians’ services during the next biennium. Collectively, these reports made it clear that there is complete agreement in all quarters that the trial year of “usual and customary” under Medicaid was a complete success, and, in a “normal year” would be continued enthusiastically and without question, but that the political problems created by the State’s desperate financial situation made it necessary to cut back on all expenditures—or, at least, give the appearance of doing so—and that the medical assistance program could not be made an exception.

Pursuant to these reports, it was VOTED that a letter be composed and sent to all members of the Society, informing them of the final decision of the General Assembly with respect to the Medicaid program, and urging them to continue to take care of the needy and near-needy in the best tradition of the medical profession under whatever arrangement are found best to achieve this end. It was further VOTED to advise all members of the Society to respond to all invitations that may be received from state agencies to participate, as individuals or

as groups, in "negotiations" to develop a fee schedule for Medicaid by suggesting that such invitations be directed to the Connecticut State Medical Society, and to inform the Commissioners of Welfare and of Finance and Control that all requests of this nature should be addressed to the Society.

Report—Delegation to HEW on Medicaid Matters

It was VOTED to accept, with commendation, a report filed by E. Tremain Bradley, Norwalk, chairman of a delegation of CSMS members who had an audience with Undersecretary John Veneman of HEW to inform him to the outstanding success of the Medicaid program in Connecticut, to advise him of the features of the program (peer review, etc.) which kept it free of abuse and reasonable in cost, and to urge that HEW grant options to states which operated successful programs during the past two years to determine the methods of payment for physicians' services best suited to those states. Currently, HEW has under study the imposition of regulations for Medicaid which would make a fixed fee schedule method of payment mandatory throughout the nation and would prohibit use of the "usual and customary charge" method by any participating state. The delegation felt that encouragement had been given by Mr. Veneman that the possibility of granting options would receive full and, if possible, favorable consideration by the panel charged with developing these regulations, but reported that no firm commitment in this regard had been made or even implied by the Undersecretary. Drs. Martin, Granoff, Weber and Polivy, who had accompanied Dr. Bradley (and Dr. Burnham of Waterbury) on the visit to HEW, added their own personal observations for the enlightenment of the Council.

Communication—Woman's Auxiliary to CSMS

It was VOTED to receive as information, and with thanks, a letter from the President of the Woman's Auxiliary, Mrs. Clarence W. Harwood, expressing appreciation to the Council for "a generous donation toward making (the Auxiliary's) 25th anniversary celebration more meaningful and enjoyable".

Communications—The Litchfield County Medical Association

(a) It was VOTED to refer a problem relating to malpractice insurance (specifically unjustified cancellation and/or non-renewal thereof by insurance agencies and/or carriers) to the Committee on Medical Economics and Insurance for study and report. The LCMA members, at the recent annual meeting, voted to bring this mat-

ter to the attention of the Council for consideration and action in response to the complaint of an LCMA member who had been faced with the subject problem. Dr. Brandon, a Vice-President of Aetna Life and Casualty, stated that his company has no policy which would preclude the issuance of malpractice coverage by itself (without insistence that the physician purchase other types of insurance as a contingency of issuance) except in the "gray areas" such as professional office liability coverage.

(b) It was VOTED to refer to the Judicial Committee, for study and report, the question of whether a County Medical Association and/or the Society should have a role to play in the penalties imposed on members by the Connecticut Medical Examining Board for infractions of statutes or for unprofessional conduct. The question was raised by LCMA for the reason that the LCMA membership, at the recent annual meeting, concurred in the opinion of the Association's Executive Committee that the penalty imposed on a member was too severe for the infraction of which he was adjudged guilty by the CMEB.

Communication re Unnecessary Physical Examinations, Etc.

It was VOTED to receive as information, and with thanks, a further communication from Donn C. Barton, Portland, concerning his thoughts on the matter of duplicate and excessively frequent physical examinations (for employment, school, camps, insurance, etc.) and the related question of making medical records more easily accessible to physicians, pharmacists, hospitals, etc.

It was further VOTED to ask the Chairman to assign the various parts of Dr. Barton's communication to appropriate CSMS Committees or other groups for study and report to the Council. Dr. Martin complied with this request as follows:

(a) Assigned to the Committee on Occupational Health the question of coordinating physical examinations and records associated with employment, to the end that duplicative and needlessly frequent employment physical examinations, laboratory work, etc. can be reduced to a minimum. Assigned to the Advisory Committee on School Health essentially the same question as it applies to similar examinations and records connected with admission to schools, enrollment for summer camp, etc.

(b) Assigned to the Conference Committee with the Connecticut Pharmaceutical Association the

question of circularizing pharmacists and physicians to the end that other (new, substitute) physicians attending a patient may find out from the dispensing pharmacist the exact nature and dosage of a medication being taken by the patient.

- (c) Directed to the Health Insurance Council the question of standardizing history and physical examination forms for persons making application for life insurance.
- (d) Assigned to the Judicial Committee the questions (ethical and legal) of transferring original patient records from one physician to another, either via the patient or by direct transfer from physician to physician.
- (e) Directed to the Connecticut Regional Medical Program the question of consolidating patients' records in hospitals, nursing homes, etc. to the end that such consolidated records could be made available to any qualified physician who was attending a patient for the first time or after a lapse of time.

Liaison with Connecticut Blue Cross

Having been apprised that actions of the 1969 General Assembly authorize hospital service corporations (Blue Cross) to also provide a mechanism for prepayment for physicians' services, and authorizes medical service corporation (CMS) to also provide a mechanism for prepayment for hospital services, the Council VOTED to communicate to the President of Connecticut Blue Cross, Inc. that, in keeping with its "open door" policy, the Society will welcome a request from Blue Cross for joint discussion of the latter's plans to formulate a program of prepayment for physicians' services. Since the Council already has an Ad Hoc Committee on Liaison with Connecticut Medical Service, Inc., it is understood that this Committee will be available to CMS to discuss whatever plans for offering prepayment for hospital services that CMS wishes to bring up for discussion.

Federal Health Professions Loan Fund

The Council received information from the Yale School of Medicine, and confirmed by Dean Patterson of the UConn Medical School, that the funds presently being considered for appropriation by the Congress for medical student loans will be grossly inadequate to meet the need created by increased enrollment in existing schools and the opening of new schools. It was VOTED to take the position that the funds to be allocated to the Health Professions Loan Fund (particularly for medical stu-

dents) in the forthcoming fiscal year should be sufficient in amount to meet the increasing needs of medical students who qualify, and the increased costs of medical education and living, and to urge Connecticut's six Representatives and two Senators to do all within their power to assure that the funds appropriated are realistic in relation to such needs.

Nominees for CHPC Obstetrical Service Study

It was VOTED to receive as information, and with thanks, a report filed by Stewart J. Petrie, Derby, in which Dr. Petrie presented the results of his investigation of the proposed study of obstetrical services in Connecticut which the Connecticut Hospital Planning Commission will make and his comments on same. It was further VOTED to approve the list of nominees for service with the Technical Advisory Committee to study the project which Dr. Petrie had prepared, with several additions, and to forward the list to CHPC. The list of nominees follows:

Stewart J. Petrie, Derby, Chairman
Howard S. Eckels, Bridgeport
Robert L. Fisher, Sharon
Morley M. Goldberg, Danbury
Joseph L. Horowitz, Bridgeport
Waldo E. Martin, Milford
Robert H. Wyatt, Greenwich

N.B.: *The foregoing is a summary of the proceedings and action of the Council on June 4, 1969. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested member of the Society.*

Placement Wanted

DERMATOLOGIST—31, Board eligible, presently completing residency. Available July, 1969. Has National Boards. Desires solo, group or clinic-type practice. No present preference as to size of community.

INTERNIST—University trained, with special interest in Infectious Diseases desires private practice association with another Internist or group in Connecticut. Available on completion of military service, July, 1970. Early commitment is desired.

UROLOGIST—32, married, completing residency. Board eligible, seeks interesting professional opportunity, preferably association.

OBS-GYN—30 years of age, married, Board eligible with National Boards, wishes to practice with an associate or on a solo basis in Connecticut. Available immediately. Military obligations completed.



A little Hygrotone
chlorthalidone



can work a long diuretic day

all the way from one daily tablet to the next to help control edema and hypertension

Its prolonged action usually provides smooth, sustained diuretic effectiveness; real one-a-day dosage, right from the start; convenience and economy.

Hygroton, chlorthalidone, can cause side effects. And it's contraindicated in hypersensitivity to the drug and severe renal and hepatic diseases.

Check the prescribing information. It's summarized on the next page.

Geigy



A little Hygroton[®] can work a long diuretic day

chlorthalidone

Indications: Hypertension and many types of edema involving retention of salt and water.

Contraindications: Hypersensitivity and most cases of severe renal or hepatic diseases.

Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has been required frequently and deaths have occurred. Discontinue enteric-coated potassium supplements immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur.

Use with caution in pregnant women and nursing mothers since the drug may cross the placental barrier and appear in cord blood and since thiazides may appear in breast milk. The drug may result in fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. When used in women of childbearing age, balance benefits of drug against possible hazards to fetus.

Precautions: Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. Because of the possibility of progression of renal damage, periodic determination of the BUN is indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, the drug should be discontinued and potassium supplements given, provided the patient does not have marked oliguria.

Take special care in cirrhosis or severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.

Adverse Reactions: Nausea, gastric irritation, vomiting, anorexia, constipation and cramping, dizziness, weakness, restlessness, hyperglycemia, glycosuria, hyperuricemia, headache, muscle cramps, orthostatic hypoten-

sion, which may be potentiated when chlorthalidone is combined with barbiturates, narcotics or alcohol, aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin rashes, urticaria, purpura, necrotizing angitis, acute gout, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Other reactions reported with this class of compounds include: jaundice, xanthopsia, paresthesia, and photosensitization.

Average Dosage: 50 or 100 mg. with breakfast daily or 100 mg. every other day.

Availability: White, single-scored tablets of 100 mg. and aqua tablets of 50 mg., in bottles of 100 and 1000. (B)46-230-E

For full details, please see the complete prescribing information.



Geigy Pharmaceuticals
Division of
Geigy Chemical Corporation
Ardsley, New York 10502

SURGEON—33 years of age, specialized training in vascular surgery interested in an association or a small group type practice. Military obligations completed. Available immediately. Board certified, and has Connecticut license.

Placement Opportunities

OPENING FOR CHIEF OF MEDICINE in 496 State Veterans Hospital. Directs program of medicine, plans, organizes and supervises case histories involving medicine. Must be board eligible and be eligible for Connecticut license. Maximum age 65 years. Salary up to \$23,060 annually, plus many fringe benefits. Quarters and services available at minimal cost. Call or write Personnel Officer, Veterans Home and Hospital, Rocky Hill, Connecticut, 529-2571, Ext. 395.

WANTED: Internist for General Medical and Surgical Accredited State Veterans Hospital. Duties are those of a ward officer on a general medical ward. Applicants must be Board eligible and up to 65 years of age, if still vigorous. Salary range: \$17,980-\$22,180. Many fringe benefits. Apply Personnel Officer, Veterans Home and Hospital, Rocky Hill, Connecticut.

G.P. OR INTERNIST — for association with 2 other well-established physicians. Salary offered for first year, dependent upon experience and qualifications, then a partnership, if mutually agreeable. Fairfield County. New office building.

PEDIATRICIAN—Long-established mixed specialty clinic in Connecticut is seeking a fifth man for Pediatrics Department. Excellent salary opportunity. Two year trial before full partnership.

PHYSICIAN with wide knowledge of medicine and surgery wanted by casualty insurance company in Connecticut.

RADIOLOGIST—to associate with four radiologists; expanding hospital and office practice in Central Connecticut; remuneration negotiable leading to full partnership. Contact Albert C. Hurwit, M.D., 477 Connecticut Boulevard, East Hartford, Connecticut 06108.

G.P.—needed for community in Litchfield County. Community has a young, growing hospital, excellent public, as well as private schools within a short distance. Community is a mixture of farming, business and industry and has many summer residents, as well as permanent residents. There is also a great need for a Pediatrician and an Ophthalmologist.

For further information, Contact William J. Zehring, M.D., Chairman, Medical Procurement, Candlewood Lake Road, New Milford, Connecticut.

INTERNAL MEDICINE opportunity. East Hartford General Practitioner retiring from active practice limited to Adult Medicine. Ideal central location, Hamilton equipment. Fluoroscopy.

PRACTICE OPPORTUNITY FOR G.P. OR INTERNIST in upstate Connecticut at the foot of the Berkshire Hills. Office fully equipped available for rent, because of death of physician. Located eight miles from excellent community hospital. Norfolk, Connecticut.

PHYSICIANS needed to practice in a rapidly expanding New England community of 45,000 (18,000 18 years and younger). Nine hospitals in immediate area. Between Springfield, Massachusetts and Hartford, Connecticut. Midway between Boston and New York. Sports, recreation, theatre, etc. are easily accessible. Contact C. S. Kissinger, Town Manager, Box 100, Enfield, Connecticut 06030.

PHYSICIAN for Emergency Room in 75 bed community hospital in northwestern Connecticut. Up to 40 hour week. Full cooperation from panel of staff physicians who cover E.R. Room for remaining time. Must be eligible for Connecticut license. Full time service approx. \$30,000 annually. Reply: Robert L. McDonald, M.D., Roxbury Falls Road, Roxbury, Connecticut 06783.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Doctor's Office

Irving H. Krall, M.D., announces the association of Vernon J. Allport, M.D. for the practice of allergy at 99 Pratt Street, Hartford.

Eugene L. Quinto, M.D., announces the opening of an office for the treatment of eye diseases at 111 Gillett Street, Hartford.

Edward Howe, M.D., Daniel E. Mack, M.D., Joseph N. Russo, M.D., William Tripp, M.D. and LeRoy Wardner, M.D., announce the opening of an office for the practice of obstetrics and gynecology at 5 Mountain Road, Suffield.

Burton Meisner, M.D., announces the opening of an office for the practice of general surgery at 257 E. Center Street, Manchester.

SUMMARY OF PROCEEDINGS
HOUSE OF DELEGATES — ANNUAL MEETING
Hartford, Connecticut — May 13-15, 1969

Reports and Addresses

The House received reports and/or addresses from the President, the Secretary, the Treasurer, the Chairman of the Council, the President of the Woman's Auxiliary to CSMS and the Chairman of the Board of Directors of COMPAC. Also received with great interest were the remarks of Welfare Commissioner Bernard Shapiro concerning his efforts to restore the "usual, customary and reasonable charge" method to the Medicaid program during the next biennium. The membership report of the Secretary and the address of the President appear at the end of this summary.

Elections

A full slate of officers, committees, representatives and advisors was elected for the terms prescribed by the Bylaws.

The officers elected are:

President: Stevens J. Martin, Hartford
President-Elect: Morris A. Granoff, New Haven
Vice-President: Frederick C. Weber, Jr.,
Greenwich
Secretary: Reginald C. Edson, West Hartford
Secretary: David A. Grendon, Sharon
Speaker of the House: Kenneth F. Brandon,
Hartford
Vice-Speaker of the House: Frank K. Abbot,
Waterbury
Councilor-at-Large: Charles Polivy, Hartford
AMA Delegate and Alternate
(January 1, 1970 to December 31, 1971)
Delegate: Norman H. Gardner,
East Hampton
Alternate Delegates: Orvan W. Hess,
New Haven

Confirmation of Interim Appointments

Interim appointments made by the Council were confirmed as follows:

AMA Delegate: Michael A. Dean, Bridgeport, to replace Max Caplan, Meriden, deceased, for the balance of the term January 1, 1969 to December 31, 1970.

Alternate AMA Delegate: Orvan W. Hess, New Haven, to replace Michael A. Dean, Bridgeport, for the balance of the term January 1, 1968 to December 31, 1969.

Presentation and Awards

1969 CSMS Press Awards:

Press awards consisting of a bronze plaque and a check in the amount of \$150 were presented as follows:

To Ned Thomas, *New Haven Register* — for competition among newspapers with over 50,000 circulation.

To William A. Walden, Jr., *Norwalk Hour* — for competition among newspapers with circulation of 5,000-50,000.

To E. R. Miller, *Ansonia Sentinel* — for outstanding presentation of a medical subject.

AMA-ERF Grants:

Furnished by the American Medical Association's Education and Research Foundation, unrestricted grants were made as follows:

To Yale University School of Medicine—\$5,446

To University of Connecticut Medical School—\$2,374

Since 1951, AMA-ERF has distributed such unrestricted grants in a total amount of over \$20 million to some 85 approved medical schools in the United States and Canada. The fund is supported by contributions from physicians and their families.

Physician Award for Community Service:

Luca E. H. Celentano, New Haven

This award by the Society for Community Service was made this year for the first time. The handsome plaque presented to Dr. Celentano was furnished by the A. H. Robbins Co.

Presentation to Retiring President:

In appreciation of his untiring efforts on behalf of the Society and its members during the past year, Norman H. Gardner, East Hampton, was presented with an engraved silver bowl and a Past President's Pin as he completed his term in office on May 14, 1969.

Presentation to Incoming President:

An engraved gavel, symbolic of his office, was presented to Stevens J. Martin, Hartford, as he became president of the Society on May 14, 1969.

Adoption of Resolutions

Resolutions on a variety of subjects were adopted by the House of Delegates as follows:

**SUBJECT: FEDERAL CONTROL OF
PHYSICIANS' CHARGES**

WHEREAS: Experience in Connecticut with a schedule of fixed fees for payment for services rendered to Welfare patients proved unsatisfactory in many respects; and

WHEREAS: An experimental period during March 1, 1968-March 1, 1969, utilizing the principle of "usual and customary charges", served to achieve the major goals of both the Medicare and Medicaid Acts in placing the needy and near-needy into the mainstream of quality medical care; therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society reaffirm its desire to maintain the "usual and customary charge" principle in both the Medicare and Medicaid programs, and that it views with great misgivings any efforts to return to a fixed fee schedule.

**SUBJECT: SOLICITATION AND
COMMERCIAL ADVERTISING OF A
MEDICAL SPECIALTY BY LAY
CORPORATIONS IN AMA PUBLICATIONS**

RESOLVED: That the House of Delegates of the Connecticut State Medical Society reaffirm the Society's traditional opposition to the practice of medicine by lay corporations and to solicitation and commercial advertising in the practice of medicine; and be it further

RESOLVED: That the CSMS House of Delegates record its strong disapproval of the policy established recently by the Board of Trustees of the AMA which opens AMA publications to solicitation and commercial advertising of a medical specialty (pathology) by lay corporations; and be it further

RESOLVED: That the CSMS House of Delegates instruct the Society's Delegates to the American Medical Association to introduce and support a resolution at the forthcoming July meeting of the AMA in New York City which calls for a reversal of the subject policy established by the AMA Board of Trustees.

**SUBJECT: CREATION OF
AMERICAN BOARD OF ALLERGY**

RESOLVED: That the House of Delegates of the Connecticut State Medical Society endorse the creation of a primary American Board of Allergy; and be it further

RESOLVED: That the CSMS House of Delegates request the House of Delegates of the American Medical Association to urge the AMA Council on Medical Education and Hospitals to consider favorably the prompt creation of a primary American Board of Allergy, and, through liaison with the Advisory Board for Medical Specialities, Inc., urge the latter body to take such actions as may be necessary to assure the early creation of such a Board; and be it further

RESOLVED: That the CSMS House of Delegates instruct the Society's Delegates to the American Medical Association to introduce and support a resolution at the forthcoming annual meeting of the AMA House of Delegates in New York City which will accomplish the purposes of these resolves.

**SUBJECT: METHODS OF
THIRD PARTY PAYMENT**

WHEREAS: The House of Delegates of the Connecticut State Medical Society is on record as endorsing the "usual, customary and reasonable charge" method of payment for physicians' services by third party agencies; there be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society adopt the position that, as two differing methods of payment for physicians' services by third party agencies, the "contractual fee schedule" concept, as exemplified by the CMS Century Contract, and the "usual, customary and reasonable charge" concept are incompatible and mutually exclusive, and that a physician cannot logically favor both concepts but must be for one or for the other; and be it further

RESOLVED: That the House of Delegates direct that the foregoing action be brought to the attention of all members of the Society.

**SUBJECT: LIMITATION OF FREE CHOICE
OF PHYSICIAN BY THE PATIENT**

WHEREAS: Increasing numbers of physicians, members of their immediate families and relatives are enrolled in health insurance and prepayment plans which include payments for physicians' services; and

WHEREAS: Enrollment in such plans entitle physicians, members of their immediate families and relatives to the payment of medical care benefits, irrespective of whether, as patients, professional courtesy is offered or they have any family connection with physicians rendering services to them; therefore be it

RESOLVED: That the House of Delegates of the Connecticut State Medical Society endorse the principle that, under circumstances in which a valid contract exists between a patient and a third party payor, there should be no limitation made by the insuring agency regarding free choice by the patient of a licensed physician to provide services covered by such contract.

**SUBJECT: ANNUAL REPORT
OF THE JUDICIAL COMMITTEE**

RESOLVED: That the CSMS Judicial Committee be required to file a report at each annual meeting of the House of Delegates.

**SUBJECT: FORMAT FOR ANNUAL
MEETINGS OF HOUSE OF DELEGATES**

RESOLVED: That the House of Delegates urge the Council to consider the resumption of the one-day format for annual meetings of the House of Delegates.

**SUBJECT: EXPRESSION OF
APPRECIATION FOR ASSISTANCE**

RESOLVED: That the House of Delegates express appreciation and thanks to Lee Isenberg Associates and Staff for the cooperative and competent assistance rendered to the chairmen of the Reference Committees of the House in the preparation of their Committee reports.

Proposed Amendments to the Bylaws

Three proposals to amend by Bylaws were introduced. These were tabled without discussion and will be acted upon at the next meeting of the House of Delegates. The three proposals were:

(1) To establish the office of Vice-Chairman of the Council and define the duties thereof.

N.B.: At present, the Bylaws call only for the election of a *Chairman* from among the members of the Council. The Chairman's duty is to "preside at all meetings of the Council. In his absence, the President shall preside."

(2) That Article X, Section 1, Paragraph 7—Judicial Committee, Subparagraph c. (1), be amended by

the addition of the words "and the House of Delegates" after the word "Council" in line 11 and before the word "and" at the beginning of line 12; i.e., the full sentence to then read: "Its (the Judicial Committee's) decisions shall be binding on the parties concerned and specific problem considered, but shall be considered only as a presumption of the Society, binding on all members only when endorsed by the Council AND THE HOUSE OF DELEGATES and published by the Council to the membership.

(3) To dissolve the Committee on Medical Care of Veterans and transfer its duties to the Committee on Third Party Payments.

The three proposals to amend the Bylaws will be referred to the Council's Subcommittee to Study and Revise the Bylaws for study and preparation of the amendments in proper, comprehensive form for presentation to the next meeting of the House.

Reports of Reference Committees

For the third consecutive year, the bulk of the business to come before the House of Delegates was assigned to Reference Committees for hearing and recommendations. Through this mechanism, all reports of officers and committees, resolutions, etc. came to the House for final action via the reports and recommendations of the Reference Committees. While all reports were ultimately accepted by the Delegates, some of the "highlights" of the many actions taken are recorded herewith:

I. Reference Committee A

- (a) Requested the Council to investigate the reasons for non-membership in the Society by a substantial number of qualified Connecticut physicians, and to develop a methodology for encouraging such physicians to become members.
- (b) Recommended that the Council review the Society's investment program and management of reserve funds.
- (c) Commended outgoing President Norman H. Gardner on the content and timeliness of his address.
- (d) Commended CSMS Woman's Auxiliary President, Mrs. Clarence W. Harwood, on the "brevity and conciseness of her report", but noted that the succinctness of her report "belies the tremendous amount of work that has been performed by Auxiliary members and the amount of monies raised in support of scholarships, AMA-ERF, etc.". In recognition of "its extensive good works" and "the interest it has shown

in the affairs of the Society”, the House offered great commendation to the Woman’s Auxiliary and its members. Also, the House extended congratulations to the Auxiliary on the occasion of the 25th anniversary of its founding (1944).

- (e) Approved the Council’s report on “Revised CSMS Guiding Principles for County Review Committees”, amending only principle No. 5 to read: “That the source of such questions (about fees and/or utilization) may be the physician concerned, another physician, a patient, a patient’s legal relative or guardian, *an authorized representative of a patient’s estate*, or a recognized third party payor.”

II. Reference Committee B

- (a) Commended the Committee on Program of the Scientific Assembly on the quality and innovative nature of the programs developed for this 1969 meeting.
- (b) Approved amendments to the Bylaws which:
 1. Eliminates the “Panel on Physician-Hospital Mediation” and transfers its functions to the Judicial Committee.
 2. Makes permissive, rather than mandatory, Council appointment and dissolution of special committees, advisors, representatives, etc., and makes unnecessary their listing in the Bylaws.
 3. Makes the Committee on Disaster Medical Care a Standing Committee of the House of Delegates.
 4. Changes the title of “General Manager” to that of “Executive Director”.
- (c) Increased the duties of the Committee on State Blood Bank to include organ transplants; voted to thank and commend Dr. Julius C. Early, retiring Medical Director of the Connecticut blood bank program, for his magnificent administration of the program.
- (d) Approved a Council-recommended proposal to form a “CSMS Coordinating Committee for Usual, Customary and Reasonable Charges”, and to authorize such Committee, on request, to cooperate with any insuring agency which offers a bona fide “usual, customary and reasonable charge” insurance program to the people of Connecticut.
- (e) Adopted a substitute resolution on “Federal Control of Physicians’ Charges” (recorded previously in this summary under “Adoption of Resolutions”).

III. Reference Committee C

- (a) Accepted the published report of the COMPAC Board of Directors as information.
- (b) Directed that the entire Council-recommended report on CSMS-COMPAC Relations be referred back to the Council for further study, with special attention to be paid to the opinion of CSMS legal counsel regarding the various sections of the report.
- (c) Tabled Fairfield County resolution on CSMS-COMPAC Relations.

IV. Reference Committee D

- (a) Accepted a proposed amendment to the Bylaws which would dissolve the Committee on Medical Care of Veterans and transfer its duties to the Committee on Third Party Payments (recorded previously in this summary under “Proposed Amendments to the Bylaws”).
- (b) On the report of the Committee on Occupational Health, commented that “it is difficult to understand why, in our heavily industrialized state, the Committee found so little with which to concern itself”.
- (c) Adopted resolution on “Solicitation and Commercial Advertising of a Medical Specialty by Lay Corporations in AMA Publications (text of resolution recorded previously in this summary under “Adoption of Resolutions”).
- (d) Adopted resolution on “Creation of American Board of Allergy” (text of resolution recorded previously in this summary under “Adoption of Resolutions”).
- (e) Adopted resolution on “Limitation of Free Choice of Physician by the Patient” (text of resolution recorded previously in this summary under “Adoption of Resolutions”).

ADDRESS OF THE PRESIDENT

NORMAN H. GARDNER, EAST HAMPTON

As my year comes to a close, I must confess I have mixed feelings. This has been the busiest year of my life without any question. The State Society has been beset with many separate matters requiring decisions. These decisions have not always been easy to make and have required many consultations to effect.

Organized Medicine is at the point where we must now make our policy for many years to come. There is a new song in the land. It has the words of liberalism, and we hear them sung often and everywhere. It is now quite popular for people to seek security and to rid themselves of any attempt

to think out their own destinies. Social planners are having a heyday. More and more people are coming under the hypnotic spell of those who would take all our responsibilities away from us in return for the money we can earn. At the same time, they take some of our liberty. This has become such an insidious process that we are hardly aware of it. I feel sure this has been done deliberately. These people who would make all our plans and answer all our problems are well equipped to accomplish their goal of complete socialization.

Private enterprise is no longer considered to be a virtue by a vocal group which, I feel, is in the minority. Many seem to have forgotten what it really was that made this the greatest country on earth—private enterprise—the initiative of the individual who was determined to make a better life for his family and himself. Our ancestors who came to these shores were thankful to receive a piece of land where they could make a home for themselves by the sweat of honest toil. The man of the family put his hands to the plow and looked up at the heavens and said, "Thank you, Lord. From now on I can take care of myself." He didn't need anyone to tell him how to spend his money—he didn't have any. But he had more than money. He had pride. He had a vision. He had the initiative to make this the greatest country ever.

I once heard a prominent speaker refer to his father's last days in a most impressive word picture. He said that when he went to see his father, a Swedish immigrant, on what they both knew would be the last time they would meet on earth, his father took his hand. "Son, you are going to come back shortly and I will not be here. I want you to have a stone cut for me. On the stone I want to say, 'He always earned his own way. He never took a damn cent from anybody!'" Who can hear these words without feeling a sense of shame for the pettiness of some in this world, and, at the same time, without feeling a glorious pride in our ancestry?

What about organized medicine—are we going to pursue the type of medical practice that we know has worked well and has made available the finest medical care in all the world? Do we feel that what we now have is worth cherishing and continuing, or are we to be persuaded to throw it all away and give up our freedom to practice medicine as we know it should be practiced? Are we no longer to consider what is best for the patient as being of primary importance? Good medical care cannot result from heavy-handed third party interference under any guise whatsoever. It is possible that the

physician may be better off economically under government financing of medical care. He has few collection worries. Indeed, he doesn't even have to worry about setting his fee. Personally, I am firmly convinced that the disruption of the relationship between the patient and the physician is not in the best interest of either.

It is my opinion that the best and most rewarding days of the practice of medicine are over both for the patient and the physician. I am glad that I began practicing medicine when I did. It is difficult to explain what I mean by this comment, but those of you who have practiced medicine in the period of the last 35 years understand. It is a sad fact—but one we must face—that most of the younger physicians are seemingly not concerned that this climate is changing.

For more than two decades we were told that the enactment of Medicare and Medicaid and other types of medical assistance programs would eliminate the problems of the aged and the needy in the area of obtaining adequate medical attention. Yet several years after the enactment of those measures, it is claimed that there still remain small segments of the population which, for a variety of reasons, appear not to have available to them the same quality of health services to which we feel all citizens are entitled to have available. If this is so, what can we do to correct the situation? I feel that we should take the lead in efforts to locate these groups of people and assist them to the fullest extent of our knowledge and resources. It is with pride that I point out to you two experiments in medical care in depressed areas being carried out by the medical associations of New Haven County and Hartford County. These plans are evidence that organized medicine does care.

In conclusion, I would like to pay tribute to the whole office staff who have put up with my presence this past year. I own a debt to Mrs. Josephine Lindquist and to Dr. Bill Richards which I can never repay. They always made it possible for me to come up "smelling like a rose". Thanks also to Mr. Peter Villano for his help on so many occasions and to Dr. Steve Martin who, as President-Elect and Chairman of the Council, gave me much help throughout the past year. I shall never forget the loyalty of the members of the Council. We have all labored together in an attempt to make medical care better and to interpret the desires of the membership. My thanks to the eight County Associations which welcomed me so sincerely and listened so attentively to what I had to say. I shall miss visiting them. I wel-

come your new President who will be given your wholehearted cooperation. I pledge him mine.

Medicine is at a crossroads—and so is the the country. We must all serve with vigilance to keep both going in the right direction. When the time comes to speak—let us stand up together and let our voices be heard.

REPORT OF THE SECRETARY

FREDERICK C. WEBER, JR., GREENWICH

The subject of medical manpower has received much discussion in both lay publications and in professional journals. This year it is particularly gratifying for Connecticut physicians to share the pride of the University of Connecticut in its first year of the new medical school at Farmington. This is exactly the answer to this particular shortage and other schools are scheduled to begin classes in the near future. These future doctors are welcome indeed into the field of patient care.

It is obvious that physicians are dependent on an ever increasing variety of technologists lending their efforts to the care of the sick. In this expanding field a new group has received approval to fill a need in the operating room as Surgical Technicians. Military necessity has demonstrated the practicality of training technicians for this and other hospital services. These technicians are joining the graduate nurses, practical nurses, physiotherapists, laboratory and x-ray technicians and even sophisticated laboratory instruments, to fill the manpower deficit in the health care area. Another opportunity for service to the sick, employment for the diligent, and assistance to the doctor has occurred and been met.

MEMBERSHIP REPORT OF THE SECRETARY

FAIRFIELD COUNTY

Membership—January 1, 1968	978
New Members	51
Less:	
Deaths	13
Resignations	8
Transfers	2
Non-payment dues	5
	28
Net Gain	23

Membership—December 31, 19681001

HARTFORD COUNTY

Membership—January 1, 1968	1127
New Members	59
Less:	
Deaths	15
Resignations	10
Transfers	4
Non-payment dues	6
	35
Net Gain	24

Membership—December 31, 19681151

LITCHFIELD COUNTY

Membership—January 1, 1968	147
New Members	7

Less:	
Deaths	1
Resignations	2
Transfers	3
Non-payment dues	1
	7
Net	0

Membership—December 31, 1968147

MIDDLESEX COUNTY

Membership—January 1, 1968	118
New Members	6
Less:	
Deaths	1
Resignations	2
Transfers	0
Non-payment dues	1
	4
Net Gain	2

Membership—December 31, 1968120

NEW HAVEN COUNTY

Membership—January 1, 1968	1029
New Members	49
Less:	
Deaths	9
Resignations	29
Transfers	2
Non-payment dues	9
	49
Net	0

Membership—December 31, 19681029

NEW LONDON COUNTY

Membership—January 1, 1968	212
New Members	16
Less:	
Deaths	3
Resignations	1
Transfers	1
Non-payment dues	1
	6
Net Gain	10

Membership—December 31, 1968222

TOLLAND COUNTY

Membership—January 1, 1968	29
New Members	3
Less:	
Deaths	0
Resignations	0
Transfers	2
Non-payment dues	1
	3
Net	0

Membership—December 31, 196829

WINDHAM COUNTY		Less:	
Membership—January 1, 1968	74	Deaths	45
New Members	4	Resignations	56
Less:		Transfers	14
Deaths	3	Non-payment dues	24
Resignations	4		139
Transfers	0		
Non-payment dues	0		
	—	TOTAL SOCIETY MEMBERSHIP—	
Net Loss	7	December 31, 1968	3770
	3	Net Gain for year	56
Membership—December 31, 1968	71	TOTALS	
ASSOCIATE MEMBERS	9	Fairfield	1001
New Members	0	Hartford	1151
Less Deaths	0	Litchfield	147
	—	Middlesex	120
Associate Members—December 31, 1968	9	New Haven	1029
TOTAL SOCIETY MEMBERSHIP—January 1, 1968	3714	New London	222
New Members	195	Tolland	29
	—	Windham	71
	3909		3770
		Associate Members	9
			3779

Leukemia Society Of America Revises Research Grant Policy

Revisions in the research grant policy of the Leukemia Society of America Inc. have been announced by Joseph R. Bertino, M.D., Chairman of the Medical Advisory Committee on the New Haven County Chapter of the Society.

The principal change limits the annual grant application review meeting to one, in late January. Deadline for submission of grant application is now November 1, with grants approved at the January meeting effective the following July 1.

"As in the past the Society will continue its support of individuals rather than project," according Dr. Bertino said. A total of 192 investigators have been awarded \$3.5 million in grants during the past 15 years, representing a steady contribution by the Society to the broadening of the base knowledge of leukemia. In addition, these grants have played an important role in encouraging outstanding young researchers to choose a career in leukemia, and in effect, to dedicate their lives to the conquest of leukemia.

The Society awards four types of grants:

SCHOLAR PROGRAM—Five year grants totalling \$100,000 are awarded to individuals having a doctoral degree (M.D., Ph.D., D.V.M.) who have demonstrated distinct ability in the investigation of leukemia and related disorders.

FELLOW PROGRAM—Two year awards totalling \$16,000 to promising young investigators having a doctoral degree to encourage work in leukemia research.

"SPECIAL" FELLOW PROGRAM—Two year awards totalling \$21,000 to investigators who have demonstrated ability in post-doctoral research and who have become interested in working in the field of leukemia and related states.

GRANTS-IN-AID—Annual grants given only in unusual circumstances to encourage new and experimental work.

Applications may be obtained by writing to the Vice President for Medical and Scientific Affairs, Leukemia Society of America, Inc., 211 East 43rd Street, New York, New York, 10017.

WOMAN'S AUXILIARY

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PRESIDENT'S REPORT 1968-1969

Politics are still a strong force in our life today and much affects us because it involves the medical profession.

As auxiliary members we must remain alert as to our local needs and help where it is possible. We must continue learning and educating our members. We continue our educating through our delegate system. Our Auxiliary influences the activities of the Connecticut Advisory School Health Council where our delegate is now Chairman of this Council and also the bill in the state legislature SB 498 on Health Education in our schools kindergarten thru twelfth grade; the Connecticut Health League which with the Nutrients Council sponsored a meeting, "Meeting Nutrition Needs in Connecticut" and the Nutrition Council also sponsored a meeting, "The Nutritional Needs of Man Today"; "The Connecticut Health League; and of course Compac. We have some members on the Board of Directors too.

Some of the highlights of our counties activities are varied. Many hours have been spent doing volunteer service to the Pre-School Visual Screening Program, distribution of kits during Diabetes Detection Week, distribution of Meals on Wheels, to the Red Cross Bloodmobile, to "Help Line" at the Connecticut Valley Hospital, to "Coffee Hours" for the mentally ill and organizing the "Friendly Visitors" for the aged. On the international level our Auxiliary members have knitted leper bandages, collected medical and nursing books, and collected used medical instruments to create goodwill abroad. On a person to person basis one of our past presidents, a speech therapist, has continued a program of helping foreign internes and residents in requiring a knowledge of spoken "American".

The Health Careers recruitment programs were held in five communities. The goal we are seeking

is to have an auxiliary member available at every high school to be able to list the available openings in health careers, the prerequisites, the length of training and etc.

Our fund raising activities deserve recognition, through dances, card parties, theatres, and luncheons the counties were able to award numerous scholarships valued at \$5,800 to young people pursuing health careers in Medicine, Nursing, Technology and so forth. Similiar undertakings succeeded in raising \$2,403.30 for AMA-ERF.

Legislation has been one of our most active concerns this year. One of our members has been at most of the hearings on the bills pertaining to health to either support or reject the bill as advised by the Medical Society.

The editor of our Quarterly has done an excellent job, one knows immediately what the Auxiliary is doing when you read the Quarterly.

This year was our 25th Anniversary and we wish to extend our thanks to the Medical Society who helped to make our celebration, held May 6, 1969 a great success.

EMMA M. HARWOOD, President

*It's your professional privilege
to replenish your ranks...*

**Give to
medical education
through AMA-ERF**



**American Medical Association
Education and Research Foundation**
535 N. Dearborn St., Chicago 10, Illinois

OBITUARY

William M. O'Connell, M.D.
1892-1969

Dr. William M. O'Connell, former practitioner in West Haven for many years died in Hartford on April 29, 1969. Death was due to cerebral thrombosis.

Dr. O'Connell was the son of the late Michael and Ann Sweeney O'Connell of West Haven, Connecticut.

He graduated from Yale Sheffield Scientific School in 1913 and from Yale Medical School in 1917. He interned at St. Vincent's Hospital in New York.

Dr. O'Connell was a Lieutenant in the Army during World War I and Lieutenant Commander in the Navy in World War II.

Dr. O'Connell was a member of the staff at Grace Hospital and St. Raphael's Hospital, a member of the New Haven Medical Association, the Connecticut State Medical Society, A.M.A., Knights of Columbus, American Legion, International College of Surgeons and the Yale Club of New Haven.

Dr. "Bill" O'Connell was a fine looking gentleman, always impeccably groomed, and was liked by his colleagues, highly regarded by his patients, particularly in West Haven, where he was the eldest practicing physician until forced by illness to retire from practice in 1967.

He leaves his wife, Elizabeth Dougherty O'Connell, his son Dr. Thomas J. of Hartford, Connecticut, nine grandchildren, and a brother Charles M. of Miami, Florida.

Albert J. Howard, M.D.

In Memoriam

Jones, Frank S., West Hartford, Yale University School of Medicine 1928. Dr. Jones was an orthopedic surgeon in the West Hartford area for over 39 years. Dr. Jones was a Navy veteran of World War II. He was associate orthopedic surgeon at Hartford Hospital, the orthopedic surgeon-in-chief at the McCook Hospital. Dr. Jones also served on the staff of the Newington Children's Hospital and the Veterans Hospital. Dr. Jones was a member of

the Chief Medical Advisory Committee of Hartford County, Connecticut Rehabilitation Association, National Rehabilitation Association, American Medical Association, Hartford County Medical Association and the Connecticut State Medical Society. Dr. Jones died May 27 at the age of 74.

Kalman, Eugene F., Fairfield, Royal Hungarian University of St. Elizabeth (Hungary) 1923. He was a general practitioner in the Fairfield area for many years. Dr. Kalman served as a Lt. in the first world war. (Austria-Hungary). He was affiliated with Bridgeport Hospital and St. Vincent's Hospital. Dr. Kalman was a member of the American Medical Association, Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Kalman died May 10 at the age of 71.

Lane, Warren Z., Darien, Columbia's College of Physicians and Surgeons 1942. Dr. Lane was a thoracic surgeon. He was Lt. Cmdr. in the Navy. Dr. Lane was attending thoracic surgeon at St. Barnabas Hospital, New York, St. Joseph's Hospital, Stamford, Stamford Hospital, Greenwich and Norwalk Hospitals. Dr. Lane was a consultant for several firms throughout the country and had written numerous professional articles published in a variety of medical journals. He was a member of the American Board of Surgery, Board of Thoracic Surgery, a fellow of the American College of Surgeons, American Medical Association, Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Lane died May 16 at the age of 51.

Steinecke, Olga, New London, Medical College of Virginia 1925. Dr. Steinecke was a psychiatrist in the New London area for many years. She was on the senior staff of the Norwich Hospital. Dr. Steinecke was a member of the New London County Medical Association, American Medical Association, Connecticut State Medical Society and the American Psychiatric Association. Dr. Steinecke died May 20 at the age of 67.

Better Health Care Linked To Change in Education System

To provide better medical care and produce more health workers there must be drastic changes in U.S. colleges and universities, representatives of state medical societies' liaison committee with nursing were told at a recent meeting in Chicago of the A.M.A.'s Committee on Nursing.

LABORATORY NOTES

SPECIAL GI ISSUE

The GI and Laboratory Groups have set up several new procedures on a cooperative basis for securing, analyzing, and interpreting gastric and intestinal secretions. Performed on gastric secretions, duodenal drainage, or stool, these tests require extreme care in specimen collection to furnish useful data. The GI service will pass the necessary tubes, furnish appropriate instructions, and correlate the laboratory analysis with the clinical data when necessary.

Stool Fat

This is the only accurate test for steatorrhea of all types.

Procedure: The patient must be on a diet providing at least 80 grams of fat daily for 3 days before the test begins and for the duration of the test. Diet sheets and special stool containers are furnished by the laboratory. All stools passed for 3 days are collected in the container which is then brought to the lab.

Analysis: The material is thoroughly mixed on a paint shaker and an aliquot analyzed for fat content. This is extrapolated to the total 3 day mass.

Report: The total 3 day fat is reported in grams/24 hrs.

Normal: Up to 6 grams/24 hrs.

Borderline: 6 to 8 grams/24 hrs.

Steatorrhea: Over 8 grams/24 hrs.—Steatorrhea is found in cystic fibrosis of the pancreas, celiac disease and sprue.

Secretin Test

This test is used to evaluate for the exocrine secretion capability of the pancreas in patients suspected of chronic pancreatitis, carcinoma of the pancreas, or obstruction to the pancreatic ducts.

Procedure: After an overnight fast, a multilumen tube is accurately located fluoroscopically in the duodenum and intestinal secretions collected for 80 minutes before and after the injection of Secretin, the pancreatic hormone which stimulates the flow of bicarbonate and fluids.

Analysis: The pancreatic secretions obtained 20 minutes before and for three 20 minute periods after Secretin, are measured for volume and bicarbonate. The total volume of secretion is calculated per Kg. of body weight and the maximal or peak bicarbonate concentration is determined.

Report: 1) Volume of secretion post Secretin expressed in ml/Kg.

2) Maximal bicarbonate concentration expressed in mEq/L.

Normal: 1) More than 2.0 ml/Kg.

2) More than 90 mEq-HCO₃/L (Av. 108 mEq/L).

Values below these levels indicate either pancreatic duct obstruction or decreased pancreatic exocrine function. Volume tends to be decreased more with obstruction and bicarbonate decreased more with chronic inflammation.

Duodenal Drainage for Cytology or Parasites

Collection of duodenal secretions is useful in suspected cases of carcinoma of the pancreas, carcinoma of the biliary ducts or specific duodenal parasites.

Procedure: A multi-lumen tube is positioned via fluoroscopy in the duodenum and then specimens collected after either biliary or pancreatic stimulation.

Analysis: Secretions are processed for cytologic study or directly examined for parasites.

Report and Normals: Adequate cell studies are reported as negative or positive. The only parasite commonly occurring in the duodenum in this area is *Giardia lamblia*, which has been clearly established as a symptom producing pathogen.

Augmented Histamine Test

This is considered the most accurate technique for assessing gastric acid production.

Method: After an overnight fast a Levine tube is placed in the pylorus and the stomach emptied. Basal secretion is collected in 15 minute samples for one hour. An antihistamine is given at 30 minutes after the onset of collection and then after basal collection histamine is given and gastric juice aspirated for one more hour.

Analysis: All eight specimens (1 hour basal and 1 hour histamine) are measured for volume and titration vs 0.1N NaOH for mEq of H⁺. The total mEq of H⁺ produced in 1 hour of basal and 1 hour after histamine are then calculated.

Report: Basal output (BAO) in mEq H⁺/1 hour and maximal acid output (MAO) mEq H⁺/hour.

Normal: Basal Acid Output (BAO)=0-10 mEq H⁺/hr.

Maximal Acid Output (MAO)=5-20 mEq H⁺/hr.

In pernicious anemia the BAO and MAO will be 0.

Low values for both BAO and MAO occur in carcinoma, chronic gastritis, gastric atrophy, and gastric ulcer.

High values for the MAO occur in hypersecretion.

The BAO should never be more than $\frac{1}{2}$ the MAO. If it is, it suggests a Zollinger-Ellison syndrome. In simple peptic ulcer disease the BAO and MAO may both be *high* but the BAO is never greater than $\frac{1}{2}$ the MAO.

R. Barnett, M.D.
M. Floch, M.D.

Coagulation Studies

We can now perform a Factor V (Labile factor) assay. Factor V is one of the three clotting components (others: platelets, antihemophilic globulin) not well preserved in banked blood or plasma. If the factor V is below 20% of normal and the patient is bleeding, fresh blood is indicated.

Low Factor V levels are often seen with severe liver disease. A clinically significant decrease in the Factor V level will produce an abnormal prothrombin time and PTT (partial thromboplastin time). A normal prothrombin time rules out a significant Factor V deficiency.

Decreased Factor V is not generally caused by acute bleeding. Massive acute bleeding will cause low platelet problems long before a Factor V deficiency occurs.

H. Truax, M.D.

Vaccinia Immune Globulin (VIG)

This material is presently available by calling Dr. Julian Schorr, N.Y.C. 212-861-7200. When current Red Cross supplies are exhausted it can be purchased from Hyland Laboratories. Its value is in persons whose resistance to vaccinia is seriously impaired and who are exposed to vaccination.

Cerebro-Spinal Fluid

The CSF protein method we had been using gave some falsely high values due to interference by several medications (including salicylates, sulfanilamide, Streptomycin, phenacetin, and Chlorpromazine). We have therefore changed to the trichloroacetic acid turbidimetric method, which shows no such interference. The new method requires 1 cc of spinal fluid. Normal extreme values for this method are 10-53 mg%. CSF protein is normally higher in newborns, and is lower in ventricular fluid.

Although CSF chloride determinations will still be available, we discourage the ordering of this test. Gambino says: "The routine measurement of spinal fluid chloride is a waste of good technologists' time . . . and is just another example of "medical myth" carried on out of habit. At the present time the best way to diagnose CSF infections is with good bacteriologic technique, not with chloride chemistry."

S. Winter, M.D.
Roy N. Barnett, M.D., *Editor*

General Assembly Commends Doctor John M. Paul

Senate Joint Resolution No. 90. Resolution Congratulating Dr. John R. Paul. The resolution was explained by Representative Earle of the 99th District who moved its adoption. On voice vote the Resolution was adopted. The following is the Senate Joint Resolution which appears in the Journal of the House for April 2, 1969.

"Resolved by this Assembly:

"WHEREAS, Dr. John R. Paul, Professor Emeritus of Epidemiology and Preventive Medicine and Lecturer in the History of Science in Medicine at Yale University will be celebrating his seventy-sixth birthday on April 18, 1969;" and

"WHEREAS, he has served as Director of the Regional Serum Bank, World Health Organization, consultant to the Secretary of War from 1941 through 1946, consultant to the United States Public Health Service and has served the United States government in the Middle East, Japan, Korea and the Soviet Union;" and

"WHEREAS, he has served on the Research Committees of the National Foundation for Infantile Paralysis and his pioneering work in the field of polio research is in part responsible for the eradication of this dread disease;" and

"WHEREAS, he has been the recipient of numerous awards and honors including the Medal of Freedom, USA and was named to the Georgia Hall of Fame of Infantile Paralysis."

"NOW, THEREFORE, BE IT RESOLVED, that the members of this assembly unite in congratulating Dr. John R. Paul upon his seventy-sixth birthday and in commending him for his dedication and his many accomplishments during his long and illustrious medical career;" and

"BE IT FURTHER RESOLVED, that the clerks of the house and senate cause a copy of this resolution to be sent to Dr. John R. Paul as a sincere expression of the high esteem in which he is held."

MEETINGS

GENERAL

July 13-17

118th Annual Convention, American Medical Association

Americana Hotel, New York City;
Exhibits, Coliseum

AMA 53rd Annual Golf Tournament, will be held Thursday, July 14 at the Winged Foot Golf Club, Mamaroneck, N.Y. All AMA members are eligible to play; information may be obtained from J. H. Lebe, M.D., 120 Broadway, N.Y.

October 23

186th Semi-Annual Meeting, New Haven County Medical Association

Waverly Inn, Cheshire

Business Meeting, 3:00 P.M.; Social Hour and dinner to follow.

MEDICINE

September 26-27

Regional Meeting (New England, Canada) of the American College of Physicians

Mary S. Harkness Auditorium, Yale Medical School

SURGERY

September 8-November 22

12th Series of Ophthalmology Postgraduate Courses
Postgraduate Institute of New York Eye and Ear Infirmary, 310 East 14th Street, New York City

At the conclusion of the regular series, there will be a one week postgraduate course designed as a review in basic sciences in ophthalmology. Write Jane Stark, Registrar, at the Institute.

January 15, 1970

Conference, Connecticut Chapter of the American College of Surgeons

Park Plaza Hotel, New Haven

Contact: Francis M. Hall, M.D., 140 Woodland St., Hartford

The Connecticut State Medical Society offers placement assistance through the Physician Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Letter To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Dr. Nahum:

I was interested in reading the paper by Dr. Savitz in the May issue of *Connecticut Medicine* ("The Dream As A Diagnostic Aid in Physical Diagnosis", pages 309-310). It would seem that the usefulness of the patient's dream in diagnosing *physical disease* has been overlooked too often in the practice of medicine. The thoughtful physician will find in this diagnostic aid, as he becomes familiar with the technique, a very satisfying blend of both the art and science of medicine.

The psychological theory on which the scientific validity of this diagnostic aid rests is elaborated by Freud in "Metapsychological Supplement to the Theory of Dreams" (1916) from which the following excerpt is quoted:

"The 'diagnostic' capacity of dreams becomes equally comprehensible, too—a phenomenon which is universally acknowledged but regarded as so puzzling; in dreams incipient physical disease is often detected earlier and more clearly than in waking life, and all the current bodily sensations assume gigantic proportions . . . It follows from the withdrawal of all mental cathexis from the outer world back to the ego, and it makes possible early recognition of bodily changes which in waking life would still for a time have remained unnoticed."

Very truly yours,

Paul M. Sherwood, M.D.

200 Retreat Avenue, Hartford, Conn.

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

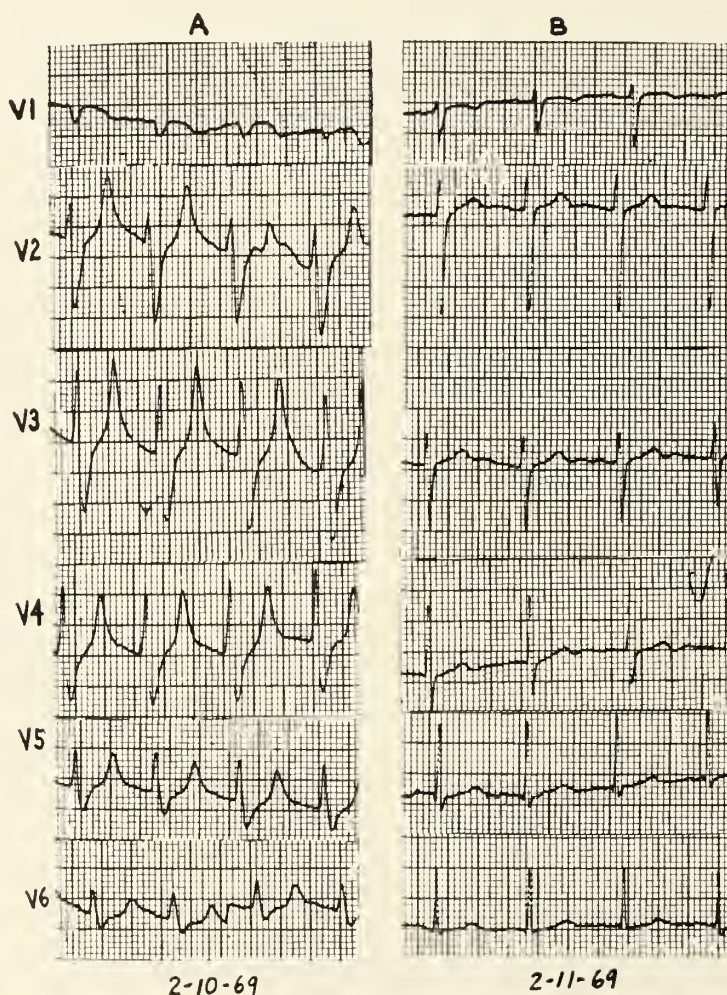
M.C., a 39 year old white female, was admitted to Yale-New Haven Hospital on 2-10-69 in a comatose state. Electrocardiogram A was obtained shortly after admission. Following appropriate therapy she regained consciousness and tracings B, C, and D were recorded on the 2nd, 3rd and 5th hospital days.

Which of the following was the most likely cause of the comatose state?

- 1) Myxedema
- 2) Overdosage with Anti-depressant

- 3) Subarachnoid Hemorrhage
- 4) Potassium Intoxication secondary to renal failure
- 5) Diabetic Keto-acidosis

The admission electrocardiogram reveals the classic patterns of hyperkalemia with absence of P-waves, prolongation of the QRS interval and marked peaking of the T-waves. The potassium level on admission was found to be 8.0 mgm.%. The patient was known to have chronic renal disease. Peritoneal dialysis was immediately instituted

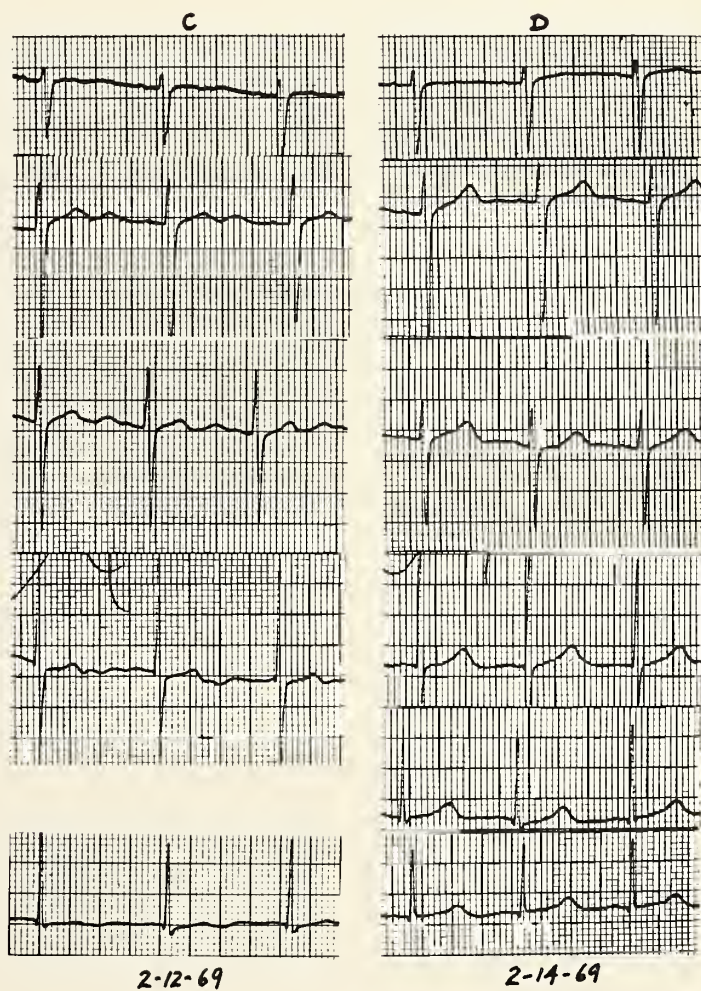


and after about 10 hours the potassium level dropped to normal levels and the patient regained consciousness. Tracing B taken at this time reveals return of normal P waves, normal QRS intervals, and subsidence of the peaking of the T-waves. Tracing C, taken on the 3rd hospital day reveals slight decrease in T-waves voltage and increase in the voltage of the U-waves, changes suggestive of low serum potassium level. This was substantiated by finding a potassium level of 2.5 mgm.%. Following appropriate therapy the potassium level returned to normal. Tracing D, taken on the 5th hospital day reveals normal T-waves and subsidence of the prominent U-waves.

Electrocardiographic changes may occur following overdosage with some tranquilizers and anti-depressants, but these changes usually consist of inversion of the T-waves and at times prolongation of the QT interval. If, however, renal shutdown results from the drug intoxication, the potassium levels may rise and changes typical of hyperkalemia may be seen in the electrocardiogram.

Electrocardiographic changes may also occur in the absence of co-existing heart disease in patients following cerebral accidents. These changes usually consist of deeply inverted T-waves with markedly prolonged QT intervals. The QRS complexes are not widened as in hyperkalemia nor is atrial activity lost. Recently, Burch and Phillips have described changes in the electrocardiogram in patients with drug induced coma, myxedema coma, cerebral neoplasm, and subarachnoid hemorrhage which consisted of prominent upright T-waves, prolonged QT intervals and prominent U-waves. No alteration of electrolytes was found associated with these changes.

In the untreated diabetic in coma, the potassium level may be transiently elevated but rarely to the levels seen in our patient. Following therapy with insulin the potassium level may drop precipitiously as a result of the action of insulin, as the potassium goes into the tissues in the process of formation of glycogen.



Science News

Spiders, Grasshoppers And Crabs

Hartwell et al have been working for several years on plants trying to gather useful anti-cancer drugs. Microorganisms and plants have yielded several anti-cancer drugs such as actinomycin D, duonemycin and vicristine. They have now extended their search into the animal kingdom which has heretofore never been examined before for anti-cancer drugs.

Spiders, grasshoppers, crabs and centipedes are among the thousands of arthropods now being evaluated by the National Cancer Institute as possible sources of anti-cancer drugs. The evaluation is an immense task. Arthropods constitute the largest division of the animal kingdom numbering more than 1,500,000 species including about 100,000 species of insects alone. A substantial number of arthropods from North and South America and Asia have already been examined in the program. The search has produced no major success to date. Nevertheless the Cancer Institute has found that extracts obtained from certain butterflies, beetles and grasshoppers have been effective against Walker 256 carcinoma and intramuscular cancer experimentally induced in the rat.

The Institute buys the arthropods from commercial suppliers and sends them to Hartwell's group who make alcoholic and aqueous alcoholic extracts from them. The extracts are then sent to private laboratories under contract to the Institute where screening tests are made on lab animals having experimental tumors.—L.H.N. *Scientific Research*, 4: 19, April 28, 1969.

National Science Foundation Becomes Political

Disbelief and shock reverberated through the scientific community following President Nixon's rejection on political grounds of Franklin A. Long as the next director of the National Science Foundation. Long, 58 is vice-president for research and advanced studies at Cornell. He had accepted the NSF post informally but over the weekend of April 12-13 because he disbelieved in the value of ABM, he was rejected from the post.

Reaction was swift. Donald Hornig, science advisor in the previous administration said "I find it

a little shocking because all of us think of the NSF directorship as a non-political post." If this is the way scientific people are to be regarded as pure agents of the administration, it will find it much harder to get good people in government posts and those who accept will be suspect by their colleagues.

Professor I. I. Rabi of Columbia, a Nobel Laureate said "I am deeply shocked. It is unprecedented. It gives this administration a very bad start. There will be a big reaction from the scientific community: they are very upset. Now apparently it is a prerequisite to be for something backed by the President to get the job. I don't know how far it will go."

Clearly it is long overdue for the scientific community to reevaluate its permissive role in being taken over by government.—L.H.N. *Scientific Research*, 4: 11, April 28, 1969.

Clotting Reflects Physical Conditioning

Dr. Earl Ferguson reports that exercise increases fibrinolytic activity. This alteration in hemostatic mechanisms in physically conditioned individuals may be important in decreasing the incidence and severity of thrombosis, pulmonary embolism, atherosclerosis and other vascular diseases.

He examined the blood of 29 individuals before and after a standardized treadmill run and again after a month of physical conditioning. The fibrinolytic activity increased 414 per cent before conditioning and 356 per cent after conditioning. Fourteen of the patients were in better condition also as indicated by a slower heart rate during the last minute of exercise.—L.H.N. *JAMA*, 208: 956, May 12, 1969.

Male Climacteric

A clue to the "male climacteric" may be in estrogen according to Dr. Jack Geller of Albert Einstein College of Medicine. Practically nothing is known about estrogen production rates and blood levels in males. Many of the paradoxes seen in experiments with testosterone in the male climacteric might be explained when estrogen metabolism is better understood.

If there were an excess, relative or absolute levels of estrogen, this might explain both the symptoms of prostatism—a common symptom in males over

age fifty-five, and the symptoms of declining sexual function and vigor.—L.H.N. *JAMA*, 208: 950, May 12, 1969.

Calling A Halt?

As pollution of crops and foodstuffs with pesticides increases, the continued use of persistent chemicals such as chlorinated hydrocarbons, DDT and dieldrin is being challenged in Britain and the United States. Michigan and Arizona have already banned the use of DDT—the latter for a trial period while an organization known as the Environmental Defense Fund is fighting the continued use of the pesticides in a test case against the State of Wisconsin.

From the beginning of 1970, DDT will also be banned in Sweden for domestic purposes and for two trial years for agricultural purposes. In Britain the use of dieldrin and aldrin on spring sown seed has been banned since 1967.—L.H.N. *Nature*, 222: 611, May 17, 1969.

Science Takes A Beating In President Nixon's Federal Budget

Sizeable cuts were made in the budget for all science agencies. National Institute of Health has been cut 36 million, Cancer 3.5 million, Heart 2.5 million, General Medical Sciences 3.5 million. The intramural research budget was cut 2.4 million. NIH intramural research grants have been cut 7.75 million. Fellowships were cut 7 million and traineeships were cut 4 million. Physical research budget is down 4 million. Biology and Medicine is down 1.2 million. These cuts are even greater because of inflation which will actually decrease further the final effective value of the money. All this socially useful activity is deprived at a time when no real look is being taken by congress at the possible waste in the war preparation and at attempts to spend many billions annually on the ABM which most knowledgeable scientists charitably declare to be a boondoggle.—L.H.N. *Scientific Research*, 4: 12, April 28, 1969.

Man And Nature

The theme of the International Biological Programme in this country is man's survival in a changing world. Two studies involve the ecology of poor immigrant laborers moving from the deep south to such places as Chicago and New York. It also involves a study of nutritional adaptation to

the environment with particular reference to the worldwide trend of migration from rural to congested urban areas where "cultural patterns are confusing and directions of improvement not well established."

Some studies relate to the balance between nitrogen, fertilizers and nitrate pollution of food and water. Then there are topics such as farmstead windbreaks, crop production in the tropics and breeding disease resistant plants.—L.H.N. *Nature*, 223: 412, May 3, 1969.

Are Physicians Facing The Facts Of Nutrition

How aware are physicians of the threat of malnutrition and of their power to restore an organism to normal? Dr. Robert E. Olson of St. Louis University thinks that nutritional diseases are not well recognized anywhere in the world. Nutrition he thinks should be a specialty of medicine.

Preliminary results from his studies in Thailand minimize the primary role of vitamin E in Kwashiorkor anemia. Vitamin E followed iron, protein and folic acid and itself caused essentially changes in the reticulocyte production. However, the role of vitamin E in Kwashiorkor anemia is not completely discounted since it could correct a disorder present in a few of the cases observed.—L.H.N. *JAMA*, 208: 783, May 5, 1969.

What Makes Us Drink

Intake of water is regulated just as accurately as its excretion and is no less significant. In the April issue of the *Journal of Physiology*, 201: 349, 1969, Fitzsimons described the way in which extracellular stimuli can induce drinking. He reduced the venous return to the heart by ligating the inferior vena cava of the rat. The animals drank substantial quantities of water which was abolished when he removed the kidneys.

The essential role of the kidney in this effect seemed to be due to renin, the hormone released from the juxtaglomerular cells of the kidney. This hormone is converted to angiotensin which stimulates release of aldosterone. Thus renin produced in response to reductions of blood volume not only stimulates sodium retention by the kidneys under control of aldosterone but instigates replacement of lost fluid by drinking.

Furthermore, angiotensin seems to be involved in the thirst mechanism, for infusion of this substance also causes rats to drink.—L.H.N. *Nature*, 222: 419, May 3, 1969.

INTERACTIONS OF ORAL ANTICOAGULANTS WITH OTHER DRUGS

Both potentiation and inhibition of anticoagulant activity have been observed in patients taking other drugs along with coumarin anticoagulants. Coumarins can also affect the activity of other drugs. Interactions have been reported less frequently with indandione anticoagulants. No method is available for predicting the occurrence or degree of interaction. Its extent may vary greatly from patient to patient, mainly because of differences in rate of metabolism; interactions have, in some cases, been serious enough to cause death.

Mechanisms of Drug Interaction—Some drugs increase microsomal enzyme activity in the liver, thus stimulating metabolic degradation of the coumarins and reducing their anticoagulant effect; patients are then likely to need larger amounts of anticoagulant, and when the drugs are discontinued, the dose of the anticoagulant may have to be reduced (S. A. Cucinell et al., *Clin. Pharmacol. Ther.*, 6:420, 1965). The drugs most clearly implicated in reports of such interactions are phenobarbital and chloral hydrate; other drugs with a potential for microsomal enzyme stimulation include other barbiturates, glutethimide (Doriden), meprobamate, griseofulvin, and haloperidol (Haldol). Phenyramidol (Analexin) may inhibit the metabolic degradation of anticoagulants and thus increase their effect.

Potentiating effects may also occur with drugs that displace the anticoagulant from protein binding sites in plasma, thus greatly increasing the peak concentration of free coumarin (P. M. Aggeler et al., *New Eng. J. Med.*, 276:497, 1967). Drugs having this effect include phenylbutozone (Butazolodin), oxyphenbutazone (Tandearil), clofibrate (Atromid-S), diphenylhydantoin (Dilantin), and salicylates.

Sulfisoxazole (Gantrisin, and other brands), chloramphenicol (Chloromycetin), tetracyclines, neomycin, and possibly other antibiotics may prolong prothrombin time in patients on oral anticoagulant drugs, mainly by interference with vitamin K production by gut bacteria. Quinine, quinidine, norethandrolone (Nilevar), and dextrothyroxine (Choloxin) also increase the anticoagulant effects of coumarin, though the mechanisms are unclear.

Potentiation Effects of Coumarin on Other Drugs—Coumarins elevate serum concentrations of diphenylhydantoin, probably in inhabiting enzy-

matic degradation of diphenylhydantoin in the liver. Diphenylhydantoin toxicity has been reported in patients receiving both drugs (J. M. Hansen et al., *Lancet*, 2:265, 1966; N. O. Rothermich, *Lancet*, 2:640, 1966). Coumarins also potentiate the hypoglycemic effect of tolbutamide (Orinase) apparently by inhibiting its conversion to carboxytolbutamide in the liver (M. Kristensen and J. M. Hansen, *Diabetes*, 16:211, April, 1967).

Conclusion—Careful attention to the dosage of oral anticoagulants is required both during administration and following withdrawal of drugs which potentiate or inhibit anticoagulant effects. Preferably, the concurrent use of anticoagulants and interacting drugs should be avoided. (For a recent review of "Pharmacological Implications of Microsomal Enzyme Induction" see A. H. Conney, *Pharmacol. Rev.*, 19:317, September, 1967.)

Reprinted from The Medical Letter on Drugs and Therapeutics, New York, N.Y. Vol. 11, No. 22.

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AROUND THE STATE

New Haven County

Board of Governors New Haven County Medical Association

The Board of Governors of the New Haven County held its second meeting of the new year on Thursday, June 5, 1969 at the Colonial House in Hamden. Twenty-six of the thirty-five members, plus guests, were present.

Dr. James H. Root, Jr., of Waterbury was appointed New Haven County Delegate to Tolland County. Dr. Stewart J. Petrie of Derby was appointed New Haven County Delegate to Windham County, and Dr. Elliott Mayo of Waterbury was appointed a member of the Program Committee.

Telephone listing complaints from Hartford County were reviewed and adjudicated.

Councilor Stewart J. Petrie reported the activities of the Allied Medical Services Committee; the CRMP Advisory Council physician nominees by the Connecticut State Medical Society, and the functions of the various scientific sections of the Connecticut State Medical Society.

The activities of the Conn. Hospital Planning Commission in the field of over-utilization of maternity service in Connecticut was outlined.

Dr. Petrie introduced the forthcoming plan to have a photograph available of each member of the Connecticut State Medical Society under a low-cost plan developed through the Executive Director's Office.

Much of the discussion of the evening centered about the problems and the very real accomplishments of the New Haven County Medical Association Review Committee. Additional help for this very busy committee has been authorized. A clearly proclaimed determination to guarantee "reasonable" fees in New Haven County was voted by the Board of Governors with a mechanism provided to implement this determination.

The orientation program for provisory members being inducted into the Association was re-designed to be both more streamlined and more meaningful.

The County office has been expanded and funds were appropriated to add to its equipment and services.

A considerable portion of the meeting was devoted to a discussion of a public relations program and initial projects were authorized for implemen-

tation. Consultation with the 1,028 members of the New Haven County Medical Association as well as with the 400-600 non-members in the county will be provided. The first step in an expanding program of contact with the local medical societies was initiated.

Dr. Morris A. Granoff of New Haven, President-elect of the Connecticut State Medical Society, resigned as Associate Councilor and was commended warmly for his services in that post. He will be succeeded by Dr. James H. Root, Jr., of Waterbury. Dr. Howard Spiro of New Haven was appointed as a Delegate and will join the Board of Governors.

Plans were instituted to study the full ramifications of pre-paid medical care programs as regards the effects they will have on the pattern of delivery of medical care in the New Haven County area.

A social hour and a "working dinner" followed with guidelines for the Public Relations Committee being the subject of a really comprehensive dinner discussion.

Respectfully submitted,
WILLIAM L. WEST, M.D., Clerk

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NEW BOOKS IN REVIEW

COLLATERAL CIRCULATION IN CLINICAL SURGERY. Edited by D. E. Strandness, Jr., M.D. W. B. Saunders Company, Philadelphia, London, Toronto, 1969. 633 pp. with 242 illustrations. \$18.50.

Reviewed by: LOUIS H. NAHUM

The main impetus for investigation into the important area of collateral circulation has been the parallel development of arteriography and direct arterial surgery. The result has been a clear recognition that the extent of the functional desirability that accompanied an occlusion was the location of the disease and the available collateral pathways. As experience was gained it became apparent that preservation of the available collateral pathways was essential to prevent further ischemia should the operative procedure undertaken fail.

We find in this book considered in detail those diseases in which a consideration of collateral circulation is important. In most instances this involves diseases that have as a counterpart the development of collateral circulation such as extremities, neck, heart, and abdominal viscera. However, there are pathologic processes such as thoracic aortic aneurysms in which the proper planning of therapy depends upon knowledge that very little collateral circulation develops in response to the lesion. In arteriovenous aneurysms an area thoroughly covered in the text of course collateral circulation is not the basic problem.

In each area of the circulation discussed, attention was devoted to normal anatomy, to congenital variations and the available collateral pathways. The discussions are well integrated with consideration of the signs and symptoms as they pertain to disease, location and collateral circulation. In the case of subclavian artery stenosis it is not a case of collateral circulation but of diversion of blood from the vertebral to the axillary artery. The title of "subclavian steal" syndrome to this clearcut disorder is quite unphysiologic since the obstructed subclavian can hardly "steal."

The application of modern study techniques is covered in detail. Especially excellent is that of the coronary circulation. This is not a book for those who need familiarity with the technical aspects of the operative procedures or approaches. It is a more basic book and certainly will be useful not only to the experienced physician, vascular surgeon and surgical specialist, but also to the fledgling house officer and to the student in physiology interested in the circulation and especially if he intends to engage in further study in this field.

The general conclusions of this book could well be summarized by John Hunter's statement that "Vessels go where they are needed." But the pathophysiology of the atherosclerotic process that has led to the burgeoning in this surgical field is practically bypassed and the mechanisms of auto-regulation and collateral circulation are quickly passed over. In fact auto-regulation does not even appear in the index. Such potent chemicals that dilate vessels distal to a stenosis as potassium, carbon dioxide, oxygen, and bradykinin are not considered. Accordingly we find the orientation is not so much physiological but surgical.

The authors are undoubtedly leaders in the field of vascular surgery, five of them out of Washington State Univer-

sity. The writing is sometimes over verbose as on page 18. "Although the sympathetic nervous system innervates all blood vessels with the exception of the capillaries its major regulatory control is at the level of the arteriole"—could be the major regulatory control of the sympathetic is at the level of the arteriole.

One must not cavil at such redundancy since the book itself is excellent and a rich reference source for a wide spectrum of medical scientists.

SURGERY OF THE ADRENAL GLANDS. By Lawrence W. O'Neal, M.D. C. V. Mosby Company, St. Louis, 1968. 295 pages. \$19.50.

Reviewed by IRA S. GOLDENBERG

Although the adrenal glands were first described in 1563 by the Roman anatomist, Bartholomaeus Eustachius Sancto-severinatus, their physiological function was not defined for centuries. The first connection between the adrenals and human disease was delineated in 1855 when Addison noted his now-famous insufficiency syndrome and shortly thereafter the first adrenalectomies were performed in animals by Brown-Sequard. Human adrenalectomy came in 1888 when a functioning neoplasm of the gland prompted a London surgeon to successful extirpation. Only in recent decades has the mystery of adrenal function been solved partially and today adrenalectomy successfully alleviates a large group of problems.

All internists and surgeons should be interested in adrenal pathophysiology, and in this slim volume Dr. O'Neal has done an admirable job of assembling almost all our present day knowledge of the embryology, anatomy, biochemistry, diagnosis and therapy of adrenal dysfunction. He discusses details of these areas, but maintains easy readability throughout the book. Several of the author's associates have contributed to the volume and, in particular, there is an excellent chapter on the role of roentgenology in adrenal disease. An exhaustive bibliography follows each chapter and little of the world's adrenal literature seems omitted.

The Mosby Company is again to be commended for quality workmanship, including excellent topography and clarity of illustrative material. Only praise can be tendered this book for both makeup and content although I wonder if the average physician, be he internist or surgeon, will find this a rewarding twenty-dollar addition to his library. It seems rather a significant reference source for any institutional medical library.

TODD-SANFORD CLINICAL DIAGNOSIS BY LABORATORY METHODS. 14th Edition. Edited by Israel Davidsohn, M.D. and John Bernard Henry, M.D. W. B. Saunders Company, Philadelphia, 1969. 1308 pp. with 698 illustrations. \$24.00.

Reviewed by: S. WINTER

This latest edition of Todd-Sanford, like the previous edition, is a work of multiple authorship. The editors have drawn on twenty-nine contributors from the fields of pathology, laboratory medicine, microbiology, biophysics, and internal medicine, to ensure complete coverage in sufficient

depth of the ever-expanding field of clinical pathology. This rapid expansion is indicated by the increase in contributors from 18 to 29, and in pages from 1020 to 1271.

Again, the topics with widest practical application have been emphasized. Sections dealing with hematology, medical microbiology, and clinical chemistry have been greatly expanded. The theory and application of radioactive isotopes to clinical medicine are dealt with in greater detail. The chapter on statistical tools has been considerably expanded. Endocrine measurements are described in considerable detail in an entirely new chapter. The growing reliance on instruments is reflected in another new chapter devoted entirely to spectrophotometric instrumentation. Examination of amniotic fluid is considered for the first time in this new edition. An entirely new and well-illustrated chapter is devoted to the growing science of cytogenetics. The chapter on hospital epidemiology is comprehensive and demonstrates good common sense.

The subject matter is generally well organized and presented in readily digestible manner. The illustrations, although frequently of small size, are clear and include a sprinkling of excellent colored plates.

The new edition will prove invaluable to all physicians, medical students, and technologists seeking a reference book for the latest advances in clinical pathology, as well as for old and established laboratory methods. It continues to fulfill its role as the single most useful work for the clinical laboratory.

PRINCIPLES OF BIOCHEMISTRY by Abraham White, Philip Handler and Emil L. Smith. McGraw Hill, New York, 1968, fourth edition, 1187 pp., with illustrations. \$17.50.

Reviewed by: H. B. VICKERY

A fourth edition of this valuable textbook has appeared after only four years and the necessity of preparing it is a vivid illustration of the rapidity with which biochemistry is advancing. The authors have skillfully condensed and eliminated, revised and expanded with the result that only 70 more pages of text have been added, but they have nevertheless brought the book up to date. The student may study a section dealing with some active topic in biochemistry with reasonable assurance that he is prepared to turn to the current literature. As an illustration of the necessary expansion, the amino acid code required only three pages in the third edition but in the fourth requires more than eleven. Comparison of the treatment of most topics shows carefully conceived additions and reorganizations.

An entirely new first chapter has been added in which the scope of biochemistry is discussed with brief reference to the history of the major fields of investigation. The emphasis in present day biochemistry is upon the composition of living tissue, the mechanisms employed in the transformations of these substances, the sources of the energy involved and the means whereby the transformations are controlled. The answers to the many questions that have arisen are, for the most part, the product of research of the past two decades.

The appearance of this new edition of a text that is presently enjoying wide use, and the assurance from its authors that is modeled and designed as the result of their own years of experience in teaching medical students in three outstanding and widely separated medical schools of necessity raises questions in the mind of any thoughtful practicing

physician. Just how much biochemistry must a young man or woman know in order to be entrusted with the responsibilities of medical practice. The authors obviously feel that they should know a great deal. Or, if they do not know it in full detail, they must know enough about it to recognize a situation which biochemistry may help them to understand. The book thus serves as a source of wide general information to which one may turn with confidence.

The text is divided into six main parts. The first deals with the major constituents of cells, carbohydrates, lipids, proteins, and nucleic acids. Then come sections on catalysis and metabolism, on blood and specialized tissues, on the biochemistry of the endocrine glands and a final section on nutrition. Many sub-sections end with discussions of the diseases or symptoms which may result from failure of the biochemical mechanism dealt with to follow a normal course, a feature of the book which greatly increases its value to the medical student or practicing physician. An index running to 122 pages greatly simplifies its use. This is a textbook which can be unhesitatingly recommended.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

The Evolution of Preventive Medicine In The United States Army, 1607-1939. Edited by Stanhope Bayne-Jones, M.D. Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Editor in Chief, Colonel Robert S. Anderson, MC, USA. Office of the Surgeon General, Department of the Army, Washington, D.C., 1968. 255 pp. with 3 appendixes, 39 illustrations, and a comprehensive index. \$2.50. Is available for purchase from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

Your Community Hospital. Edited by Robert E. Walsh. Beacon Press, Boston, 1969. 286 pp. \$5.95.

Medical Interviewing: A Programmed Manual. Edited by Robert E. Froelich, M.D. and F. Marian Bishop, Ph.D., M.S.P.H. The C. V. Mosby Company, St. Louis, 1969. 116 pp. \$4.75.

Introduction To Medical Science. Edited by Clara Gene Young and James D. Barger, M.D., F.A.C.P. The C. V. Mosby Company, St. Louis, 1969. 295 pp. Illustrated. \$7.95.

Medical Supply In World War II. Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Editor in Chief, Colonel Robert S. Anderson, MC, USA. Editor for Medical Supply, Charles M. Wiltse, Ph.D., Litt. D. Office of the Surgeon General, Department of the Army, Washington, D.C., 1968. 662 pp. with 149 illustrations, 54 maps, 8 tables, and a comprehensive index is available for purchase at \$8.25 a copy from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

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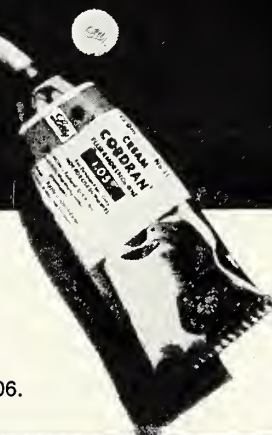
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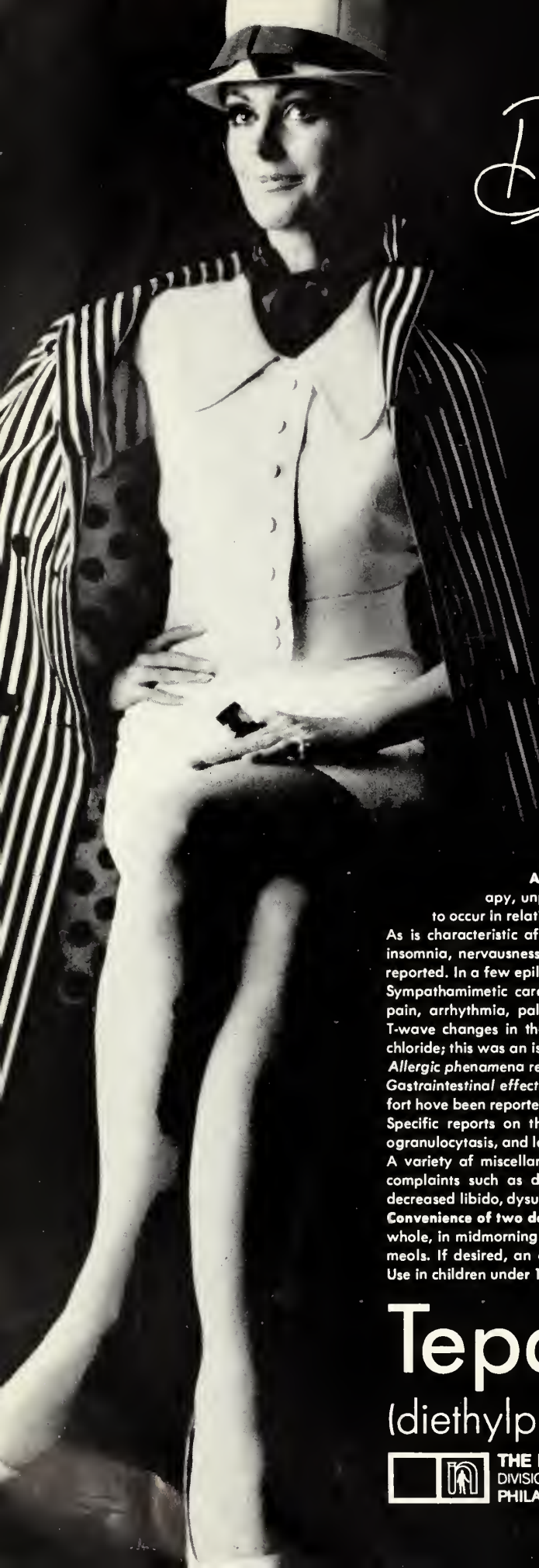
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Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema. Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported.

Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia.

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Connecticut Medicine

editorials

On Chemical Warfare

At Ypres in 1915 during the first gas attack the Germans slaughtered 5,000 French and created a gap in the line filled with a gasping and disorganized mob. (see front cover) But the Germans failed to exploit their advantage. From then on for three and one-half years both sides settled down to plastering each other with chemicals to no obvious advantage except to retaliate. Out of this exercise in beastly futility the United States Army Chemical Corps was born.

Seymour Hersh has written his book to show what has happened to this organization since its creation. For forty years the Chemical Corps which has produced no visible signs but smoke, is now emerging as a giant. Since 1918 three nations have used Chemical Biological Warfare (CBW), the Italians in Abyssinia, the Egyptians in Yemen and the United States in Vietnam. The Chinese accused the United States of using germ warfare in North Korea, but this was never proven. On each occasion there was no fear of retaliation. On each occasion there was no military advantage. On each occasion there was a reaction by a nauseated world and we are now in a phase of that reaction against our Government's action in Vietnam. Books appear, protests grow forcing the defenders of CBW to explain its powers, necessity and even "humanity."

Three books have appeared at about the same time. One a series of papers by experts on Chemical and Biological Warfare. Its Scope, Implications and Future Development.¹ It contains a concise series of technical reports in five sections: weapons, uses, research policy, legal aspects and ethical problems. It is a powerful collection of facts written by an international group of scientists. Another is by Brown,² an army man recently transferred to Vietnam! The study traces United States, British, German and Japanese Chemical Warfare policies and preparations from the first to the second World War in an attempt to learn why CBW was not studied more. He concludes that it was too difficult to employ and enemy retaliation made the game not worth the candle.

Coming up to the present, Brown offers his views on the restraints against United States employment

of lethal chemicals in Vietnam where retaliation is not a significant factor. His shocking acceptance of CBW in areas where retaliation is not possible, aside from its moral depravity is not even based upon reality. What about possible retaliation with gas rockets or mortar shells on Saigon or United States base camps. Shall we encumber United States forces with masks and protective suits and to face demands for those items by the frightened population in Saigon.

Has Brown and presumably the Army considered that mortar cartridges and rockets loaded with nerve agents could place insurgents at a sizeable advantage over government forces. Such weapons are in our arsenals, why can they not be in our adversaries. They weigh no more than rockets and shells now being used. Relatively light toxic weapons able to cover large areas could serve the guerrilla well, for he often knows the location of the opposing forces and it less often knows his. Brown nevertheless is against prohibition of initiating CBW and it seems ominous that he should now be transferred to Vietnam.

The other, Hersh's book³ concentrates on the American achievements in CBW. He generates his indictment of the CBW "boondoggle" mainly from a detailed cutting of government reports and newspaper stories. Hersh covered the Pentagon for the Associated Press and quotes from unnamed sources within the establishment as well as from official releases. It contains information on the development of United States Policy, budget and bases. He gives a tragic account of the propaganda effect on behalf of the CBW boosters, their success in the universities and how they achieved respectability.

In the words of Patrick Wall "it takes a remarkable organization to flourish for fifty years under continual attack without a single success to its credit unless gassing the Vietcong first and then plastering the victims with explosives from overhanging B52's can be considered as success."

At first the Chemical Corps was justified as a necessary preparation for retaliation. In 1964, the New York Times wrote "It is a long established policy that chemical and biological agents will never be used except in retaliation for a chemical biological attack." Evidently that policy is no longer established and the change of policy has

given new life and prosperity to CBW. Since the United States can't risk using its nuclear weapons and its near defeat of its armed forces using conventional weapons, there is temptation on the part of the military to play the supposed ace of CBW up their sleeve. The untried weapons of CBW offers the tantalizing promise of ultimate "humane" weapons in a casualty free war that spares the real estate.

Hersh's book provides much of the evidence that this view is nonsense. CBW promises rather to speed cheap, dirty, uncontrollable action and counteraction if released. If not released, it is tying up more and more of the world's scarce health facilities in a secret biological arms race, that should not and need not take place.

Weapons with the radical potential of chemical and biological agents deserves deep study by competent people other than the military and their scientists. Wrong decisions can have major effects on the nature of the military, political and health environment we face for years after they are made.

L.H.N.

References

1. Chemical and Biological Warfare: Its scope, implications and future development. Edited by Steven Rose. Harriap, London, 1968. The report of the London Conference on CBW.
2. Fredric J. Brown: Chemical Warfare. A Study in Restraints. Princeton University Press, Princeton, N.J. 1968. xx to 35 pp. \$9.00.
3. Seymour M. Hersh: Chemical and Biological Warfare: America's Hidden Arsenal. MacGibbon and Kee, London, 1968. 354 pp. \$6.00. Published in the U.S. by Bobbs-Merrill, New York.

Agents To Prevent Sunburn

New demographic and epidemiologic evidence indicates that exposure to sunlight is a major cause of "aging" of the skin and of the basal-cell carcinoma and squamous cell carcinoma found in exposed skin.¹ It follows that if a preventive program is instituted early in life especially of fair-skinned persons who sunburn easily, by effective preparations it should make it possible to prevent or minimize the degenerative cutaneous changes actinic keratosis and carcinoma that develop as the result of prolonged or repeated exposure of unprotected fair-skin to sunlight.

An evaluation of various agents and their effectiveness to prevent sunburn has recently been published by Pathak and his associates.² Various methods have been used to prevent actinic injury to the

skin since 1922 when it was recognized that in man sunburn and suntan are caused by the action of a narrow band within the ultraviolet spectrum. The most widely used is the topical application of a material that because of absorption of light or opacity or both, will screen out impinging erythemogenic radiation.

Many preparations that effectively screen out the ultraviolet rays from artificial sources under laboratory conditions fail to protect against sunlight under outdoor field conditions. They are easily removed as the result of sweating or altered chemically by impinging solar radiation. Most are readily removed when the skin has been immersed in water a few minutes.

Pathak et al studied the protective value of 24 commercially available sunscreen preparations and various chemical agents that have long been known to absorb ultraviolet light. They studied fair-skinned persons undergoing long exposure (over four hours) under natural sunlight, when subjects undergo exercise accompanied by profuse sweating, subjects after bathing or swimming. They studied subjects under intensely bright sun with hot dry climatic conditions (during the months of July and August in the Northern Hemisphere, 40° N. latitude). Finally they studied subjects on the snow-covered mountains at high altitudes that reflect ultraviolet radiation causing sunburn of the exposed parts of skiers.

They found that 5 per cent paraamino benzoic acid in 70-95 per cent ethyl alcohol (MAP) and 2.5 per cent isoamyl dimethylamino benzoate (Escalol 506) in 65-95 per cent alcohol (preparations G and K) are by far the best sunscreen preparations. After a single application they can protect fair-skinned people under a variety of sun exposures noted above. Moreover the preparations only partially inhibit tanning and allow immediate pigment darkening as well as melanogenesis by long wave ultraviolet and visible radiation. Finally the preparations are cosmetically acceptable being invisible and without odor or color on the skin.

Differences in the resistance of the various sunscreens to elution during swimming were striking. After a 15-20 minute swim of the 24 lotions tested MAP, G and K were the only sunscreens that gave any effective protection during exposure to solar radiations. In these tests, G and K proved to be even more effective than MAP. They appeared to remain on the horny layers of the skin and continued to provide excellent protection against the

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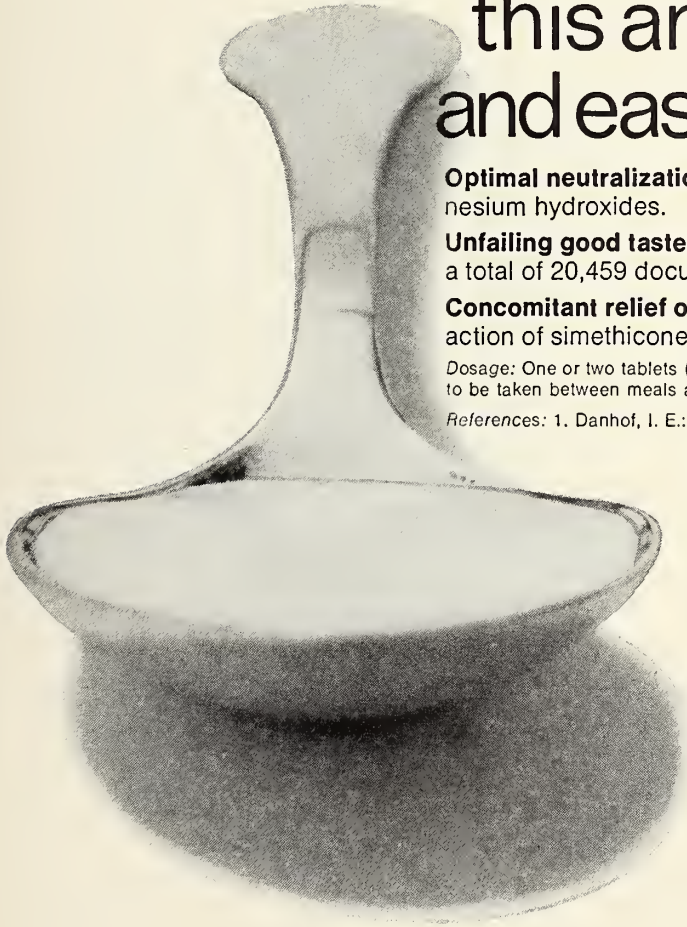
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References: 1. Danhof, I. E.: Report on file. 2. Hoon, J. R.: Arch. Surg. 93:467 (Sept.) 1966.



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solar energy received during 90-120 minutes of exposure, while MAP gave satisfactory protection for 60 minutes of exposure after swimming.

In the tests made in Switzerland MAP and preparation G provided excellent protection against the exposure of the snow reflected sunlight encountered on skiing slopes. These preparations can definitely reduce the hazard of facial sunburn for skiers and mountain climbers.

The laboratory and clinical findings reported here do not reveal any new sunscreen agents since MAP has been used for over 40 years as topical sunscreens. The unique finding of Pathak's investigation is the remarkable ability of MAP, G and K to protect normal human skin from the harmful effects of intense erythemogenic solar radiations.

L.H.N.

References

1. Urbach, F., Davies, R. E. and Forbes, D. P.: Ultraviolet radiation and skin cancer in man. In *Advances in Biology of Skin: Carcinogenesis*. Proceedings of a symposium held at the University of Oregon Medical School, 1965, Vol. 7. Edited by W. Montagna and R. L. Dobson, New York, Pergamon Press, 1966. Pp. 195-214.
2. Pathak, M. A., Fitzpatrick, T. B. and Frenk, E.: Current concepts: Evaluation of topical agents that prevent sunburn. *New Eng. J. Med.*, 280: 1459, June 26, 1969.

The Methadone Treatment For The Criminal Addict

Just

There is now a reasonable concern for the mental health and attitude of a person as it affects him and his social condition. When human behavior, whatever its origin, leads a human being to physical or emotional suffering or poverty or conflict with society and its values then psychiatry seeks by therapy or persuasion to influence human behavior in directions of health and away from suffering, poverty or conflict with society.

There is at present no effective medical treatment for criminal or violent behavior, alcoholism, drug addiction, sexual deviation, juvenile delinquency and a host of other disorders of human thinking and physical conduct. Because there is not available effective treatment medicine asks for more research. On the other hand society is anxious for immediate social action whether or not we know what to do. There is pressure everywhere that something should be done immediately about disorders of human behavior of which drug addiction is only one example. Deviant or maladaptive behavior may actually be a disease as we in medicine have come to think of disease.

Deviant human behavior will be understood sooner and adequate prophylactic and therapeutic measures both medical and social will be earlier at hand if we accept the responsibility of the treatment of medical complications of drug addiction, alcoholism and other forms of human behavior. The responsibility for the detoxification of the intoxicated patient as well as the problem of studying the physiologic basis of human conduct is our task. It is on this context that the article by Dole and his associates¹ is an excellent example of a scientific study of the medical treatment of disordered human behavior in a small number of criminal drug addicts. Many more are needed.

The potential motivation of criminal addicts for methadone treatment was tested in a New York City Correctional Institute for men. Of 165 inmates seen all with records of five or more jail sentences, 116 applied for treatment after a single interview. None of them had previously made application to the methadone program. Of 18 randomly selected from all applicants with release dates between January and April 1968, 12 were started on methadone before they left jail and then referred to the program for after care. None of them became re-addicted, to heroin and 9 of the 12 had no further convictions during the 50 weeks of follow-up study. All of an untreated control group became readdicted after release from jail and 15 of 16 were convicted of new crimes during the same follow-up period.

The relevance of these findings to the total population of criminal addicts obviously depends on the validity of the sampling techniques.² However, if any biases crept in they were probably to reduce not to exaggerate the indexes of acceptance and success of the methadone treatment. Assuming that the prisoners seen in this study were typical recidivists, criminal addicts, a view supported by the corrections officers as well as the statistics of Dole's study, it can be said that the methadone program provides a way to stop the criminal behavior in a large population of addicts. The overall success in motivating and rehabilitating criminal addicts thus appears to be at least 50 per cent.

This report holds promise for a successful palliative treatment for drug addiction. If the customary recidivism is not permanently avoided but only postponed after a follow-up period of 5-10 years then the treatment program will require evaluation in the light of its test and the value of postponing as opposed to alleviating recidivism in hard-core addicts. Data bearing on this question should soon

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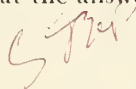
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be forthcoming for Mayor Lindsay has just announced that in New York a non-profit corporation to be directed by former United States Attorney General Nicholas de B. Katzenbach will "test approaches to methadone maintenance with the goal of treating 5,000 addicts over a five year period."³

By such means social agencies will be funded to do their job of maintaining social welfare of their clients at a high level of human dignity. The rehabilitative services will be funded and in turn fully accept their responsibility for rehabilitating the addict and criminal. Education will be brought into the picture by accepting this task of effectively informing and training their students, and the public about human behavior, its development and its maladaptations. It will also require social scientists to devote their efforts to the study of human behavior as well.

Through this entire venture into new areas we must keep squarely in view the difference between fact and speculation and strive to recognize the difference between hypothesis and conclusion.² The reason is that society insists on immediate social action whether or not we know what to do, whereas science insists on research to get at the answers.

 L.H.N.

References

1. Dole, V. P., Robinson, J. W., Orraca, J., Towns, E., Searcy, P. and Caine, E.: Methadone treatment of randomly selected criminal addicts. *New Eng. J. Med.*, 280: 1372, June 19, 1969.
2. Patch, V. D.: Human behavior, medicine and social reform. *ibid* 1415.
3. Johnston, R. J. H.: City plans clinics to treat addicts. *The New York Times*, May 30, 1969, p. 1.

New Drugs Active Against Tuberculosis

Two latest additions to drugs active against tuberculosis are ethambutol and rifampicin. Ethambutol is given by mouth and peak levels of about 5 micrograms per ml. are obtained by a dose of 25 mg. per kg. Its action is bacteriostatic. It is well tolerated. However, side effects do occur very rarely (in 3 out of 100) consisting of retrobulbar neuritis with reduced visual acuity and constriction of peripheral fields. Controlled studies have compared isoniazid with ethambutol and ethambutol with PAS. The results indicate that 15-25 mg. per kg. of ethambutol is as effective as 10 gram sodium PAS in daily regimens with 300 mg. isoniazid. With the ethambutol regimen suited to a particular patient sputum conversion is possible in all cases. Accord-

ingly it is an attractive drug for patients in whom previous treatment has failed.

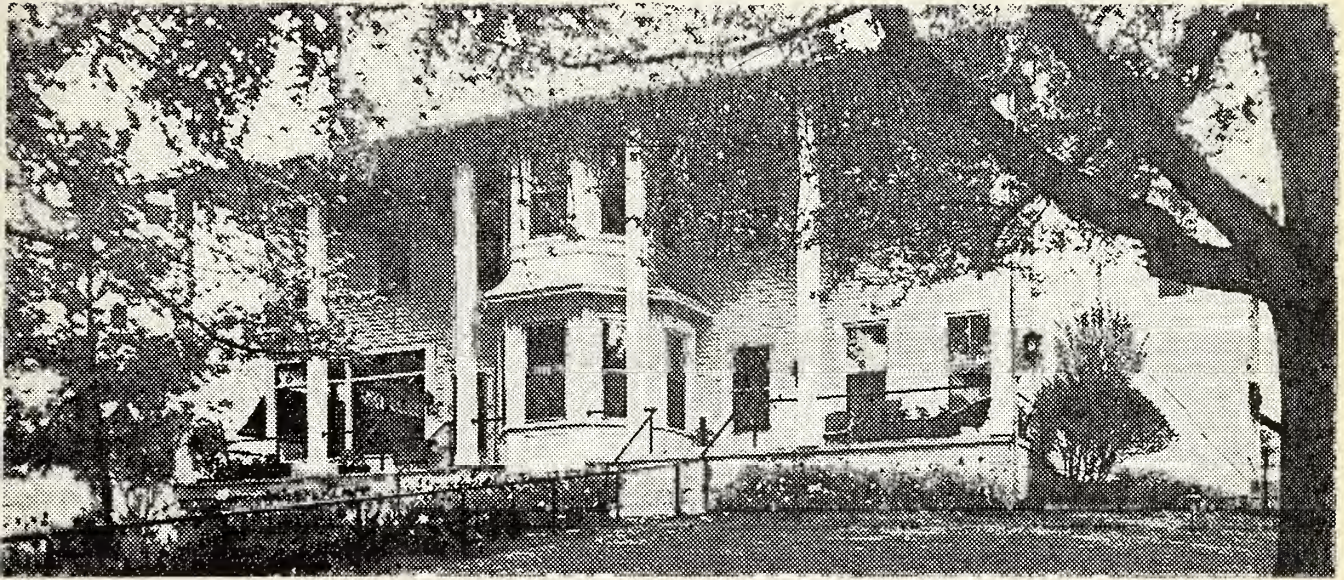
Rifampicin is derived from an antibiotic rifomycin B produced by the fungus *Streptomyces mediterranei*. It is well absorbed from the gastrointestinal tract and gives peak concentrations of 8 micrograms per ml. 2-4 hours after ingestion of 600 mg. These concentrations will be increased in the presence of liver damage and accordingly it is recommended that it not be used in alcoholics.

More than 100 reports have been published on the use of rifampicin in man. All agree it is remarkably free from toxicity. Present advice is against its use in women during the first three months of pregnancy. *Lancet* reports that Baronte and Lukinovich gave 450 mg. daily for 4-5 days to 11 patients in whom previous drugs had failed. At the end 3 had negative cultures and 8 positive but 5 were less sensitive to rifampicin than before treatment. A less satisfactory method but one that raises no ethical difficulties is to add the drug to a regimen of other drugs which had apparently failed to reduce the number of bacilli. *Lancet* reports Pine's results on 6 cases so treated and after one month 4 were negative and after 12 months 5 were negative. The conclusion is warranted that rifampicin is active against tuberculosis in man and may even be as highly active as it is in experimental tuberculosis in mice.

It is now time for properly controlled trials and such trials for both ethambutol and rifampicin have been started under the egis of the Medical Research Council. Until they are complete it would be wise to reserve judgment and not to include either drug in an initial treatment regimen unless toxicity, hypersensitivity or intolerance make the well tried streptomycin, isomazid, and PAS unacceptable. Experimental evidence suggests that both drugs may have an important role in the future. Ethambutol is especially potent in guinea pigs. Rifampicin plus isoniazid may be a uniquely powerful combination and has sterilized the lungs in experimental tuberculosis in mice after 4 months treatment in all animals.

There appears to be two important factors concerning rifampicin. The blood levels are more than 100 times necessary to inhibit growth in vitro and the higher the concentration at which a drug acts on a multiplying population of bacilli, the more rapid and thorough is likely to be the destruction of bacilli. The other point is that most wild strains of tubercle bacilli have a remarkably small proportion of rifampicin resistant mutants. Conse-

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quently the risk of emergence of resistant strains is less during treatment.

These important properties of rifampicin may eventually make possible one of the major goals of chemotherapeutic research; the shortening of treatment necessary to achieve permanent arrest of the disease. That this is possible can be demonstrated only by large and long controlled trials. Certainly no routine shortening of treatment with any regimen is at present justified.

Both ethambutol and rifampicin as of now seem likely to be valuable additions to the antituberculosis drugs. The rifampicin derivatives are active against a large number of organisms other than the tubercle bacillus and also against some viruses in vitro. Accordingly we must be aware that their use in such cases might render unrecognized tuberculosis cases resistant.

Both rifampicin and ethambutol are presently very expensive. The cost of one year treatment with rifampicin is about 500 dollars and with ethambutol 250 dollars. Clearly until the cost can be drastically reduced these drugs can make little contributions to the control of tuberculosis in the poorer countries where most of the worlds tuberculosis cases live.

L.H.N.

Transplant Psychosis

Over 100 heart transplants have been done and the results so far are dismal. The average length of life after transplant is not much greater than without transplantation. We have been told that treatment of the rejection process and resulting infection is the gravest immediate threat. We have not been told what the patient himself who underwent the operation suffered postoperatively.

Now Scientific Research¹ reports on the psychological effects of transplant surgery. The problem of psychosis in recovery room from open heart surgery is now well documented.² At a meeting of the American Psychiatric Association, Dr. Donald T. Lunde reports from Shumways team at Stanford on five of thirteen heart recipients who developed postoperative psychosis. Dr. Lunde points out that brief psychotic states are quite common among patients who undergo open heart surgery. They last two to three days, occur a week or so after the operation, involve a state of delirium and visual hallucination and disappear when the patients leave the recovery room.

The psychotic reactions of the heart transplant patients have a longer duration, as long as six weeks, and there is a change in the patient's mode of thinking and perception of himself. Three of the psychotic transplant patients at Stanford became paranoid and refused to take medicine because they believed the nurses were trying to poison them. One suffered from delusions of grandeur picturing himself as a world celebrity. Of the five who became psychotic four died without regaining mental stability. The fifth snapped out of his psychosis after a month.

In his report Lunde suggested several factors might have contributed to the patient's psychotic behavior—the psychological trauma of the surgery itself, the isolation of the intensive care period, the eerie sight of faceless figures in gowns and masks and the steroid drugs that are given in large doses to combat tissue rejection. While there is no positive link between steroids and psychotic behavior, doctors have observed somewhat similar disturbances in other patients who receive large doses of steroids for other illnesses. Furthermore, as the transplant is performed in a patient with good histocompatibility the need for steroids could correspondingly decline.

Obviously a lot more study needs to be done. Several questions at once present themselves. Are these reactions due to the transplant itself or to drugs? What relation do steroids have to depression? How frequently do these reactions occur and what doses of steroids are the patients taking? How psychologically meaningful is the heart as an organ? Is it losing one's own heart or having someone else's heart in you? We clearly need more collaboration between psychiatrists and transplant teams.

Theoretically the ideal way to study the relationship of steroids to emotional disturbances would be to observe one group of patients who are taking steroids and another group who are not. This, however, is presently impossible because no one is willing to do heart transplants without steroids. A study of those truly histocompatible patients requiring little steroids might furnish the answer to this problem but there are too few of these. In any event this question cannot be solved statistically since the number of heart transplant patients here and elsewhere in the country is too small to say what the statistical likelihood of a psychotic reaction is.

L.H.N.

References

1. Transplant psychosis needs research, *Scientific Research*, 4: 11, June 23, 1969.
2. Nahum, L. H.: Madness in the recovery room from open-heart surgery or "they kept waking me up." *Conn. Med.*, 29: 771, November 1965.

Fun And Games To Cut Coronary Risk

University faculty participation and perseverance in a physical training program in Madison, Wisconsin indicate that such programs can be enjoyable, sustain interest and at the same time reduce risk factors in coronary heart disease. The university professors in the study were considered a good example of a population "at risk." At the initiation of the program in January 1967 the subjects selected for study ranged from 45-49 years of age. Many were corpulent and inactive and there was almost unanimous dislike of exercise.

Telephone interviews with 496 faculty members produced 380 volunteers for a medical screening examination. They were recorded for weight, blood pressure, serum cholesterol levels, electrocardiogram, resting heart rate and aerobic power. The initial examination eliminated 14 volunteers who were considered too high a risk for the program. An additional 196 were removed because they did not have sufficient risk factors.

Of 170 professors who qualified for the program with two or more risk factors 101 attended an orientation session and 97 decided to participate. Thus only about half of the subjects that might have benefitted agreed to participate. Volunteers were assigned to one of three types of activity groups.

Activity in group I included walking, jogging or running three times a week. A minimum of energy expenditure was planned for group II. Emphasis was placed on relaxed activity without organized play. During meetings men engaged in many light activities including "frizbee" throwing and walking. The group planned as a control was supposed to meet only once a week. However, these men became so interested they also met on their own two or more times a week.

Vigorous games were planned for group III which met three times a week. "All forms of human motion were included in the group games which were chosen with an emphasis on having fun."

During the first three weeks activity periods were limited to a maximum of 30 minutes and gradual-

ly increased to 45 minutes. Selection of activities for all the groups was left to the invention of instructors who supervised all activity. Each volunteer was given a thorough medical examination every four to five months.

As of December 1968 participants had lost an average of 5 per cent of their total body weight, showed a slight decrease in blood pressure and a 10-12 per cent reduction in serum cholesterol levels. The volunteers also showed a 20 per cent increase in maximum oxygen intake capacity. There also appears to be a significant increase in all participants work capacity as indicated by increased ability in a treadmill test.

Of the original 97 participants nearly one-third showed minor electrocardiogram changes including ectopic beats and slight S-T segment depression which disappeared after two years.

The other studies are sponsored by the Public Health Service, one at the University of Minnesota and another at Pennsylvania State University using a cross section of the entire university population.

The data from all three studies will be analyzed at the University of Michigan Ann Arbor to determine the feasibility of such training programs for the prevention of heart disease.

If this movement will catch on in other universities we can expect a new wave of physical conditioning by making exercise fun. Most of us brought up in a comfortable and sedentary civilization actually develop and use only a fraction of our potential cardiac reserve and in the process accumulate risk factors of coronary heart disease.

L.H.N.

Reference

1. An intellectual's plan to cut coronary risk. *JAMA*, 208: 1279, May 26, 1969.

Is Hong Kong Strain Influenza A New Virus?

The influenza viruses were first cultivated only in the 1930's and that is only a few major influenza epidemics ago. It is possible, however, to deduce something about the viruses which were current before then by studying antibodies in human sera. Such deductions depend on the well established immunological principle that once the antibody forming mechanism has "been primed" with a certain antigen it produces antibodies against the antigen and goes on doing so even when stimulated by other antigens which are only distantly related to it. This

phenomenon in relation to influenza has been called "original antigenic sin."

A group of workers associated with the late Professor J. Mulder of Leyden have made a number of interesting contributions to this kind of retrospective serological epidemiology and further findings are in Mulder's paper.¹ The earliest experiments showed that the sera from the people who were children in 1890 had antibodies against Asian A2 strain and that slightly younger subjects had antibodies against a virus recently epidemic in horses A/Eqi 2.

After this was confirmed by other workers it was reasonable to conclude that the epidemic of 1890 was probably caused by a virus related to A2 strains and there then followed a period of prevalence of a virus related to the horse virus. Masurel's new observations support and extend this view. They are based on tests on over 3,000 sera collected in 1957 and also just before the present Hong Kong epidemic. They show that the antibodies against A/Eqi 2 in the sera of old subjects have apparently been boosted by A2 virus infections in the past ten years.

Most impressive, however, is the fact that when sera collected in 1957 were tested with A2 Hong Kong virus the sera in subjects over sixty proved to have a high incidence of antibody against this strain. Masurel's work has shown that A/Eqi 2 and A2 Hong Kong are antigenically related, so it is not surprising that these sera also contain some antibodies against A/Eqi 2. The relationship between Hong Kong virus and the A/Eqi 2 viruses is supported by other work. A virus related to both A/Eqi 2 and Hong Kong was circulating between 1890-1918 when persons now over age fifty were alive.

It would be unwise to conclude that there is an exact correspondence between the antibody found in sera and the timing of antigens of influenza epidemics in the past. But it seems reasonable to conclude that the 1957 influenza pandemic may have been similar to the pandemic of 1889-1890 and the virus of Hong Kong '68 epidemic may be closely related to the virus which followed the "A2 pandemic" at the turn of the century.

It now looks as though the history of influenza has repeated itself. The sequence of epidemic serotypes which has affected us in the past decade probably occurred at the turn of the century. Until recently we thought the influenza virus was always surprising us. Epidemiologists can look more discriminatingly into the future by understanding the history of the past. The patterns of influenza will

not always remain mysterious, for Hong Kong strain is really not new. We had it with us many years ago.

L.H.N.

Reference

1. Mulder, N.: Relation between Hong Kong Virus and former human A2 isolates and the A/Eqi 2 virus in human sera collected before 1957. *Lancet*, I: 907, May 3, 1969.

Vitamin A Acid In Psoriasis And Other Scaling Dermatoses

Young animals fail to grow epithelial cells in cell structures and undergo keratinizing metaplasia in vitamin A deficiency. For this reason vitamin A in the form of the free alcohol or one of its esters has been administered for years both topically and systemically for hyperkeratotic skin disorders in humans but with highly variable results. Topical administration of preparations containing another form vitamin A acid has been shown to decrease scaling in "ichthyosis" and other scaling dermatoses. However, those laboratory animals and humans with actual vitamin A deficiency in which scaling of the skin is present, recovered and their skins cleared when vitamin A was added to the diet. There is, however, no evidence for vitamin A deficiency in most patients with scaling dermatoses and the results topically administered vitamin A in such patients have not been satisfactory.

There are three types of vitamin A, the alcohol, aldehyde and acid. Bern et al¹ and Fisher applied vitamin A alcohol to rat and human epidermis and found a two-fold thickening of the granular layer of the epidermis. Vitamin A acid was found to be effective in ichthyosis when topically administered but in the .1 per cent strength it was not always efficacious. Frost^{3, 4} tried it upon 26 patients with psoriasis and found much improvement but they used .2 per cent vitamin A acid and the beneficial effect was equally good when it was applied in a petrolatum base as in a cold cream base and the improvement lasted for 10 to 14 days.

Irritation in the form of erythema and on occasion itching occurred in one out of ten patients with a .2 per cent and in one out of four treated with 0.3 per cent. In either case the erythema resolved rapidly if medication was withheld for one to two days. It usually did not recur if the frequency of medication was decreased. Frost quotes von Stüttgen to the effect that vitamin A acid was more effective than vitamin A palmitate. Frost investigated whether the therapeutic effectiveness is a

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function of rate of transport through the human skin. He concluded that this cannot be the factor in effectiveness because vitamin A acetate with much greater mobility through the skin is much less effective therapeutically than is vitamin A acid.

Frost and his group found that topical administration of vitamin A acid was most effective therapeutically in psoriasis, lamellar ichthyosis and epidermolytic hyperkeratosis. As yet the mechanism of action for the topically administered vitamin A acid in therapy of these dermatoses is unknown. However, the conditions showing the greatest response were those in which epidermal cell hyperplasia is present. While the effect may be of the keratolytic type, the diminution of erythema in psoriasis and improvement in epidermolytic features evident in Frost's histologic sections of skin specimens which vitamin A acid can induce suggests a more complex action in these disorders.

It is evident that further basic and clinical studies are required to define the role of vitamin A acid in the management of scaling dermatoses.

L.H.N.

References

1. Bern, H. A. et al: The influence of vitamin A on the epidermis. *Amer. J. Anat.*, 96: 419, 1955.
2. Fisher, L. I.: Some effects of topical vitamin A upon human epidermis. *Arch. Derm.*, 75: 667, 1957.
3. Frost, P. and Weinstein, G. D.: Topical administration of vitamin A acid for ichthyosiform, dermatoses and psoriasis. *JAMA*, 207: 1863, March 10, 1969.
4. Weinstein, G. D. and Frost, P.: Abnormal cell proliferation in psoriasis. *J. Invest. Derm.*, 50: 254, 1968.

Another Look At The Results Of Cardiac Transplantation

Messmer et al report on what happened to 15 patients who underwent cardiac transplantation for end-stage heart disease. The mean survival time averaged 111 days but this included 22 days of waiting for operation, so that the mean survival time after operation was 89 days. The mean survival time of the 42 potential recipients who could not obtain a donor was 74 days. The question at once presents itself whether this difference justifies wide clinical application of cardiac transplantation.

Of course, a basic goal of medical therapy is to improve a patient's condition. An analysis of Messmer's figures reveal that some patients "felt better" after transplantation as a result of an improved cardiac output and their positive mental attitude helped them to enjoy the time they lived with the

allografted heart. Some even left the hospital. We are not told, however, how much suffering all the patients endured from treatment of the rejection process.

One of the main problems of course is lack of donors. Too many must die before a donor becomes available. The pressure to save life led to the use of a xenograft in one desperate case and in others without having a suitable tissue match. These died promptly from acute rejection as could have been anticipated. Rejection is still the major problem in cardiac transplantation and is dependent in part upon the tissue compatibility. Clearly the first step in preventing rejection is proper selection of the recipients on the basis of the tissue match.

Infection stimulated by immunosuppression is another often fatal problem. Antilymphocyte globulin (ALG) may permit reduction of doses of other immunosuppressive agents such as azathioprine and corticosteroids, but it has its drawbacks because it may be responsible for severe herpes simplex infection and for oncogenesis at the site of the infection.

Extension of life span is not as important as adding quality to life that is offered and is an important goal of medical treatment. Messmer's experience seems to be that life may be prolonged by cardiac transplantation in some patients with terminal heart disease. But the difference in mean survival time between the allografted patient and the inoperated potential recipients is not great enough to justify wide clinical application of cardiac transplantation. However, the need for further clinical experience is important enough to continue cardiac transplantation in suitable cases on an experimental basis.

When we obtain a better understanding of all the immunological problems, optimal tissue compatibility, and how to induce immune tolerance, these should help in survival as well as contribute knowledge to other medical areas.

We need more detailed descriptions as to how much post-operative suffering the patients endure. We must also not lose sight of the physiological problems that are unsolved such as severance of the nervous connections to the heart and the lymphatic drainage from the transplanted heart.

Obviously the solution to the heart problem lies elsewhere in recognizing its predisease state or its early clinical manifestation so that we may eliminate the "risk" factors that contribute to progression of heart disease to a fatal outcome.

L.H.N.

Reference

1. Messmer, B. J., Leachman, R. D., Nora J. J. and Cooley, D. A.: Survival time after cardiac allografts. *Lancet*, I: 954, May 10, 1969.

Overactive Sympathetics In Myocardial Infarction And Hypertension

The excretion of the catecholamines, adrenalin and noradrenaline is said to be increased in conditions of stress which is said to be an underlying cause of many medical conditions. Jewitt et al¹ have investigated the excretion of noradrenaline and adrenalin in patients with acute myocardial infarction and found that the mean excretion of catecholamines in nine patients who died was significantly greater than in forty-three who survived.

There were significant correlations between high levels of catecholamine excretion and the development of pulmonary edema and arrhythmias, particularly ventricular and multiple arrhythmias. No difference existed in the incidence of supraventricular arrhythmias and heart block in groups of patients who excreted different quantities of catecholamines.

Multiple type arrhythmias and atrioventricular block were significantly more frequent in patients with over 402 units of LDH. However, damage to muscle appears not to be the only factor responsible for the increase in catecholamine excretion in these patients.

There is an interesting relationship between stress, catecholamines, and blood pressure. Nestel² found that young patients with labile hypertension lack a greater reaction to mental stress than do a group of controls. The two groups were similar in age and sex distribution and the stress was a forty minute mental test given at noon. He collected urine before and after the test so that the content of catecholamine could be estimated and blood pressure was measured for four hours before the test and each minute during the first ten minutes of the test.

The hypertensives had significantly higher resting blood pressures than the controls without significant differences in catecholamine excretion. All subjects increased their blood pressure and adrenalin excretion as a result of carrying out the test. However, the increases were always significantly greater in the hypertensive group than in the controls. Systolic and diastolic pressure increased in the control group 10-15 per cent respectively. In the

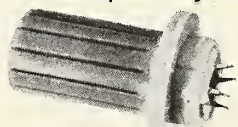
hypertensives the increases were 24 and 26 per cent respectively.

In the hypertensives, adrenalin excretion more than doubled under stress. The noradrenaline excretion by the hypertensives under stress was even greater than in the controls. Here is further proof that mental stress can increase the excretion of catecholamines and raise the blood pressure, but for some reason patients already showing signs of hypertension have an increased sympathetic nervous system response to this type of mental stress.

These two studies one on myocardial infarction and the other on hypertensive patients point up the role of the sympathetics in each of these disorders. The one on myocardial infarction is especially important because of what we already know about the role of the sympathetics in the genesis of cardiac arrhythmias.³ The operative hypothesis proposed by Nahum and his group is that cardiac premature systoles or tachycardia are the result of the interaction of two factors, the sympathetic nervous system and an exciting agent. In the case of myocardial infarction, the exciting agent is anoxia interacting with adrenalin and noradrenaline to produce the ventricular arrhythmias.

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Cardiac arrhythmias in myocardial infarction may be serious and now that we know that such patients excrete increased amounts of catecholamines, it behooves the clinician to eliminate the exciting agent, that is anoxia, and to reduce heightened sympathetic tone by every means available from sleep during the first few stressful days,⁴ to sedatives that reduce anxiety.

In addition to the production of arrhythmias the sympathetics may directly injure the myocardium if stimulated excessively. We now know of the clinical condition of "sympathetic storms" which occur in patients with cerebral hemorrhage. In such patients there are found areas of focal injury and a classical picture of STT wave changes in the electrocardiogram.⁵

L.H.N.

References

1. Jewitt, et al: *Lancet*, I: 635, 1969.
2. Nestel: *Lancet*, I: 692, 1969.
3. Nahum, L. N.: The role of the sympathetics in premature systoles. *Conn. Med.*, 30: 320, May 1966.
4. Nahum, L. H.: Sleep treatment in acute myocardial infarction. *Conn. Med.*, 32: 642, September 1968.
5. Nahum, L. H.: Cardiomyopathy from Sympathetic storms in cerebral hemorrhage. *Conn. Med.*, to be published.

Intrauterine Contraceptive Devices

Reports of adverse vascular effects of oral contraceptives (*Medical Letter*, Vol. 10, p. 66, 1968) have increased the interest in intrauterine contraceptive devices (IUDs). However, not all women can use IUDs successfully, and these devices, too, cause occasional serious complications. How IUDs prevent conception is still unknown; they apparently do not interfere with ovulation or with implantation of the embryo.

IUDs are made in a variety of shapes and sizes. Among the presently available devices that have been most widely used are the Lippes loop (Ortho) and the Saf-T-Coil (Julius Schmid, Inc.), both open devices; and the Birnberg bow (American Caduceus Industries) and the Hall-Stone ring (Glaxo-Allenburys, Ltd., England), both closed devices. All of these except the stainless steel Hall-Stone ring are made of plastic. The Majzlin Spring (Anka Research Ltd.), a newer device, appears to be as effective and as safe as the Lippes loop and the Saf-T-Coil, but removal is reported to be difficult.

Contraceptive Efficacy—Pregnancy rates during the first year's use of a properly inserted and fitted

IUD vary from one to three per cent with the Lippes loop and the Saf-T-Coil, the most reliable of the older IUDs. The risk of pregnancy declines with successive years of use. The IUDs are less reliable in preventing conception than the oral contraceptives, but they have been more reliable than condoms or diaphragms with spermicidal agents. Many women find IUDs more acceptable than topical devices that require pre-coital preparation.

Tolerance of IUDs—Older women and those who have borne several children tolerate IUDs better than younger women and those with no children. Spontaneous expulsion of the device, bleeding, and pain severe enough to require removal occur most frequently in the first four months of use. Replacement with a larger device or a different shape may result in better retention; patients with pain and bleeding sometimes tolerate a smaller device but the danger of expulsion is thereby increased. There is no evidence that IUDs cause the conceptus to implant ectopically, nor that they cause fetal abnormalities. The use of an IUD does not appear to affect fertility after it has been removed.

Adverse Effects—The most common adverse effects of IUDs are irregular or heavy bleeding and pain. IUDs sometimes cause or aggravate pelvic inflammatory disease. At least 10 deaths from acute infection, including sepsis and peritonitis, have been reported in the United States. Aseptic insertion of a sterilized device helps reduce the hazard.

Perforation of the uterus is estimated to occur about once in each 2500 insertions. Because closed types of IUDs such as bows or rings may cause herniation and obstruction of the bowel after perforation, most *Medical Letter* consultants no longer employ closed devices. An abnormally positioned uterus may predispose to perforation; therefore sounding of the uterus before insertion and downward traction on the cervix to straighten the uterus during insertion are mandatory. Since the uterus is especially susceptible to perforation during the early post-partum period, insertion is best delayed until about the sixth week after delivery. To avoid the possibility of interference with pregnancy, the IUD should be inserted during menstruation. There is no evidence that either plastic or steel IUDs have caused genital cancer.

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The Odor of Apocrine Secretion

Roy N. Barnett, M.D. and Stuart H. Bender, M.D.

Apocrine Secretion Odor

The vast attention given to the prevention of axillary odor by advertising media has not been paralleled by scientific attention to the cause of this odor. Current theory blames bacteria.¹ "It was concluded that bacterial action is necessary for the production of odor from apocrine sweat".² "When the common and uncommon axillary bacteria were micro-cultured in nutrient enriched apocrine sweat, only the resident corynebacteria and coagulase-negative micrococci were able to produce the typical axillary odor".¹ It is remarkable that the same authors found no odor of pubic apocrine glands despite an essentially identical bacterial flora.³ They believe that the pubic glands are functionless and make no sweat, therefore do not produce odors.

A major problem in studies of this type is the small volume of secretion available for study. Shehadeh and Kligman¹ note that "only a few of many subjects could deliver more than perhaps a half dozen droplets". Their study used capillary tubes of sweat; after culture "the tip was broken and the tube inserted deeply into the nostril" for smelling.

A new approach to the problem of securing adequate samples for study is through the use of fluid from apocrine cysts of the breast. Apocrine sweat gland structures have been recognized in human mammary tissue for many years.⁴ They are found in almost every normal breast and communicate, unless cystic, with the lactiferous system. Their characteristic eosinophilic epithelium differentiates them readily from normal mammary epithelium. The authoritative histochemical studies of Henry Bunting⁴ conclude "they represent apocrine sweat glands which are normal constituents of the mammary gland". Among the vast number of histochemical studies which have been performed in an effort to elucidate the mode of secretion of these sweat glands, a recent publication⁵ investigated the relation of these "apocrine-like" cells of the breast to those in the axillary apocrine glands. The conclusions were: "The main evidence in favor of the view that apocrine-like cells represent a metaplastic transformation of the mammary epithelium is the

similar histologic appearance and staining properties of the two structures. By showing that the axillary apocrine gland and the mammary apocrine-like cells also share a similar distribution of four oxidative enzymes the present study adds further support to this theory".

Material and Methods

During 1964, 1965, 1966 and 1967 appropriate material was studied as follows. Whenever a cyst 1.5 cm in diameter or larger could be felt in freshly removed breast biopsy specimens, the surface of the tissue was sterilized with 70% ethyl alcohol and the cyst fluid aspirated with a sterile needle and syringe. Most of the fluid was emptied into a Petri dish top and spread out for maximum ease of smelling. If any typical odor was noted the remaining fluid in the syringe was cultured in thioglycollate broth tubes. Culture were incubated at 36°C for 4 to 5 days and smeared before discarding. The tissue including the cyst wall was subjected to gross examination and appropriate microscopic sections studied.

During the 4 years the typical axillary odor was confirmed by the Senior author, also by three Board-certified Pathologists, several technologists and a number of student technologists and Pathology residents.

Results

A total of 13 specimens were analyzed and are tabulated in chronological order (See Table). Cultures were not made from the 3 cysts which had no odor and which served as controls for histology. The types of cyst lining seen are illustrated in the microphotographs. (Figs. 1, 2, 3, 4). There was no correlation between preservation of epithelium and degree of odor. Whenever any epithelium was recognizable it was of apocrine type. There was no inflammatory reaction around any of the cysts to suggest prior infection, and none of the cyst fluids contained bacteria which could be cultured.

Comment

The work of Bunting³ and Tremblay⁵ clearly indicates the identity of the epithelium of these breast cysts with the epithelium of axillary apocrine sweat glands, and our own studies indicate the identity of the odor produced by these cells whether in the breast or in the axilla. The lack of inflammatory reaction and the uniformly negative cultures pro-

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DR. STUART H. BENDER, Associate in Dermatology, Norwalk Hospital, Norwalk.

Surgical Number	Size of entire specimen (cm)	Largest dimension largest cyst (cm)	Odor	Culture	Histology of cyst lining (AC = Apocrine cells)
64-2889	4 × 3.5 × 2	2.5	2+	NG*	Slightly flattened AC
64-2965	3.5 × 3.5 × 3	3.0	0	None	Mostly destroyed; a few flattened AC
64-3476	8.0 × 4.0 × 2.5	3.0	1+	NG*	Almost all destroyed; a few flattened AC
65-3818	5.5 × 3.5 × 2.5	1.5	0	None	Typical AC
66-758	8.5 × 8.0 × 6.0	2.0	1+	NG*	Mostly destroyed; few clumps of AC
66-2333	10.0 × 6.5 × 4.0	2.5	±	NG*	Two-thirds destroyed; rest AC
66-3003	7.0 × 5.0 × 4.0	4.0	±	NG*	Three-fifths destroyed; rest flattened AC
66-3054	8.0 × 5.0 × 4.0	2.0	1+	NG*	Mostly destroyed; some flattened AC
66-3379	4.5 × 3.5 × 2.5	4.0	1+	NG*	High columnar typical AC
66-5183	7.0 × 5.5 × 3.0	3.0	3+	NG*	Partly destroyed; rest typical AC
66-5697	5.0 × 4.5 × 3.5	2.5	4+	NG*	Completely destroyed; no visible AC
67-777	5.0 × 4.5 × 3.5	1.5	0	None	Almost all destroyed; rare flattened AC
67-2207	13.0 × 8.5 × 1.8	2.6	4+	NG*	Almost all destroyed; few cuboidal AC

*NG = No growth; None = No culture made

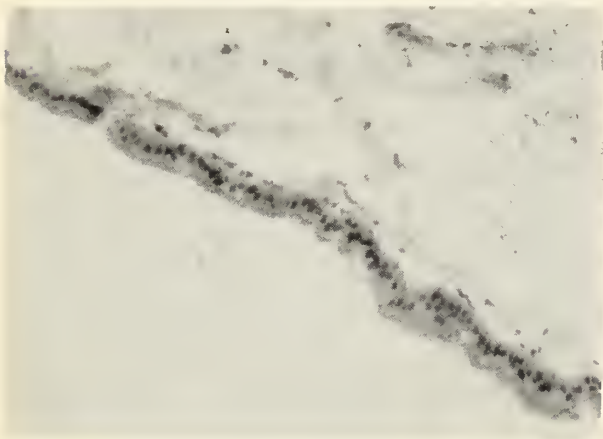


Figure 1

Typical tall eosinophilic apocrine cells with basal nuclei and pinched off apical granules. X 100

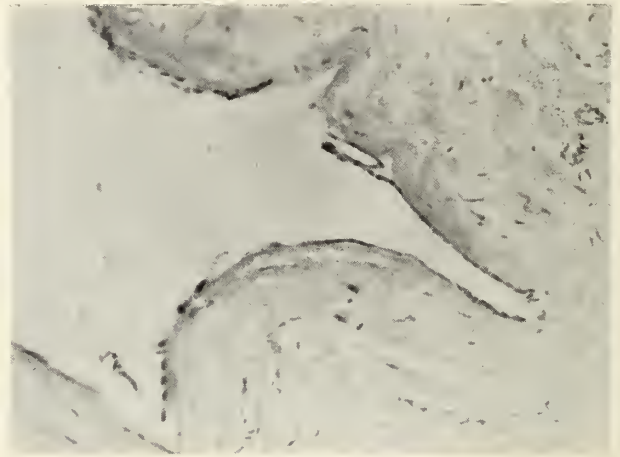


Figure 3

Apocrine cells uniformly flattened. X 100

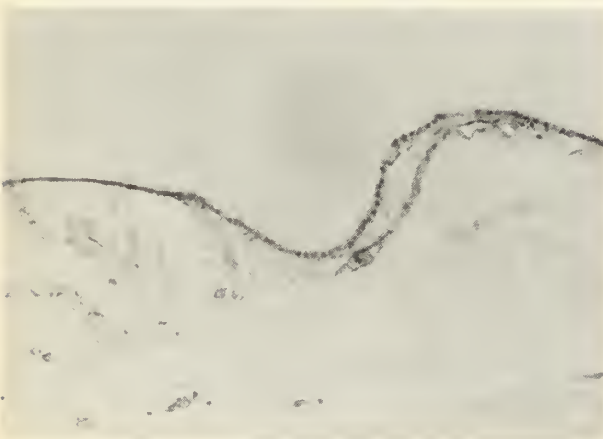


Figure 2

Apocrine cells vary from flattened to cuboidal. X 30

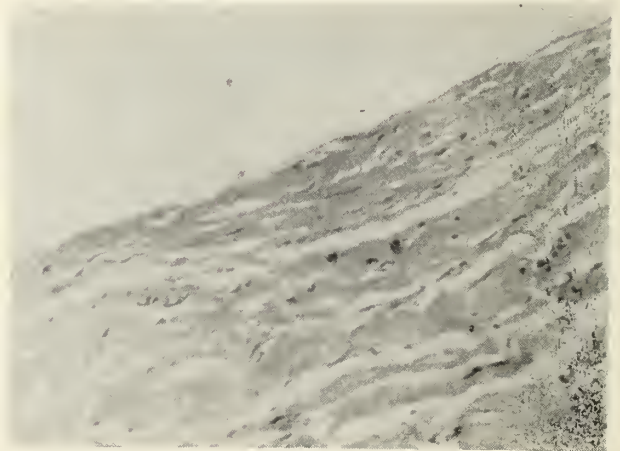


Figure 4

Apocrine cells absent except for a single flattened cell in the center. X 100

vide no evidence to implicate bacteria in the causation of the odor. The organisms implicated by Shehadeh and Kligman are all easy to culture, so the negative cultures are conclusive evidence of their absence at the time of surgery. Perhaps bacteria were present, produced the odor and later disappeared; this is conjectural and we believe most unlikely. Because breast cyst fluid is often turbid many cultures have been made in the past, both at our laboratory and elsewhere, with uniformly negative results.

Our thesis, then, is that apocrine cells in the axilla and mammary gland produce a secretion which has an intrinsic odor unrelated to bacterial action.

If it is correct, a corollary deduction is that deodorants must act effectively by inhibiting the production of axillary sweat rather than by inhibiting bacterial growth.

Summary and Conclusion

A series of breast cysts lined by apocrine epithe-

lium indistinguishable from that of axillary apocrine glands was studied. 10 of them had the typical odor of axillary sweat although none contained bacteria which could be cultured. It is concluded that apocrine sweat has a typical odor which is intrinsic and unrelated to bacterial growth.

Acknowledgment

Mr. T. Barnett processed the microphotographs Figures 1, 2, 3 and 4.

Bibliography

1. Shehadeh, N. and Kligman, A. M. The bacteria responsible for axillary odor. *II. J. Invest. Dermatol.* 41, 3, July 1963.
2. Hurley, H. J. and Shelley, W. B. The human apocrine sweat gland in health and disease. Charles C. Thomas, Springfield, 1960, p. 85.
3. Kligman, A. M. and Shehadeh, N. Pubic apocrine glands and odor. *Arch. Derm.* 89, 461-463, March 1964.
4. Bunting, H. Cytochemical properties of apocrine sweat glands normally present in the human mammary gland. *Anat. Rec.* 101, 5-12, May 1948.
5. Tremblay, G. Histochemical studies of oxidative enzymes in apocrine-like cells of the breast and in axillary apocrine glands. *J. Invest. Derm.* 50, 238-243, 1968.

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Choriocarcinoma of Fallopian Tube

John Carangelo, M.D. and Raymond A. Gagnon, M.D.

Introduction

Choriocarcinoma simulating a ruptured tubal pregnancy is a rare gynecological emergency. The following is such a case, in which the correct diagnosis was made only after microscopic examination of the surgical specimen.

Case Presentation

A 30 year old gravida 3 para 2002 white female presented with a chief complaint of vaginal bleeding and abdominal pain.

For the previous three weeks, she had noticed painless vaginal bleeding resembling a heavy period. Approximately 12 hours before admission, she experienced sharp lower abdominal pain followed by shoulder pain. Her last normal menstrual period occurred six weeks prior to admission.

Past history and review of systems were negative except for a D & C done 4 years earlier for sterility.

Physical Examination revealed a well developed, well nourished, pale woman in moderate distress due to pain. Pulse 108 — respiration 16 — Blood pressure 90/40. Positive findings were limited to the lower abdomen, with tenderness and rebound in both lower quadrants. Pelvic examination revealed bleeding through the cervix, slight enlargement and tenderness of the uterus, and a left adnexal mass. The admitting diagnosis was a ruptured ectopic pregnancy.

A D & C under general anesthesia produced very little decidual tissue. The culde-sac was tapped and free blood was aspirated. Afterwards, a laparotomy revealed 1500 cc's of free blood in the abdomen. The left fallopian tube was ruptured at the isthmus with marked proximal dilatation. A left salpingectomy and a left cornual resection was performed. The patient received 5 units of blood. Her post-operative course was uneventful. Histologic examination of the specimen revealed trophoblastic overgrowth with vacuolization. The curettings were of normal-appearing decidual tissue. A diagnosis of tubal hydatidiform mole was made, and the patient was discharged from the hospital on the seventh post-op day.

For the following six weeks, the patient continued to have vaginal bleeding resembling a heavy menstrual flow. A serum rat gonadatropin test was positive. Subsequently, she was readmitted for a repeat D & C. The curettings were of a secretory endometrium with marked deciduoid reaction.

Curettings from both procedures, and the specimen of Fallopian tube, were reviewed by Dr. Arthur Hertig of Harvard Medical School. He diagnosed the surgical specimen as "typical choriocarcinoma of the tube (without any villi)". He found the first curettings to be decidua with a little Arias-Stella change, and the second curettings pure decidua.

Approximately two weeks after the second D & C, chest x-ray revealed a soft tissue density in the left lower lobe. The patient was transferred to another institution and treatment with methotrexate was initiated. After four courses of therapy — (50 mg./day for 5 days), the urinary chorionic gonadatropin titre was still 500 International units/24 hours. Because of this sluggish response, drug therapy was switched to Actinomycin D, with good over-all results. The patient suffered with alopecia, thrombocytopenia, and severe headaches but these side effects disappeared when therapy ended.

Presently—three and one half years after the diagnosis, the patient has fully recovered. The pulmonary lesion has disappeared and the patient carries out normal daily activities. She takes oral contraceptives so that her urinary chorionic gonadatropin can be monitored as an indicator of possible recurrence of the tumor. All such studies, including the most recent in June 1968 have been negative.

Microscopy

Multiple sections from the dilated portion of the tube revealed columns of actively proliferating trophoblastic cells accompanied by severe hemorrhage with surrounding coagulation necrosis. There was marked anaplastic activity of both the cystotropho-



Figure 1

Actively proliferating trophoblastic cells with invasion of the tubal wall and a vein containing tumor embolus.

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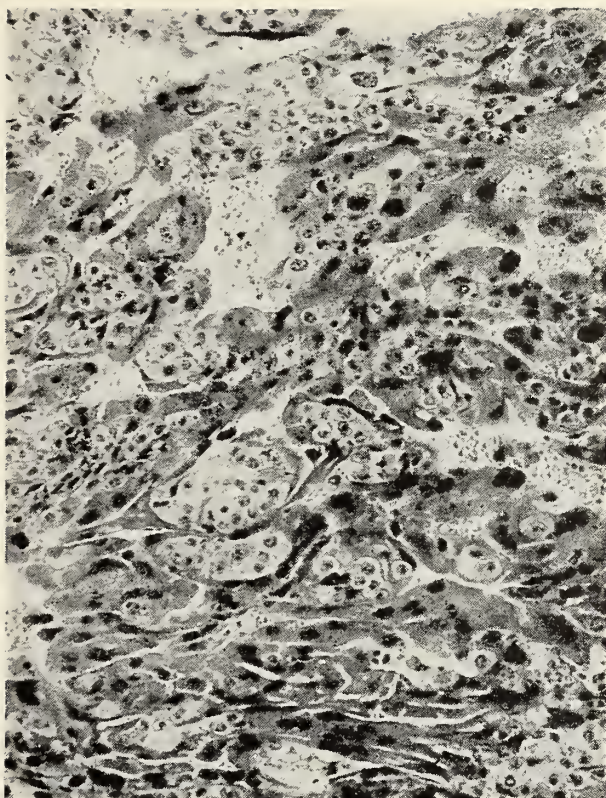


Figure 2

Higher magnification of the syncytial cells and cytotrophoblasts. Vacuolization is noted.

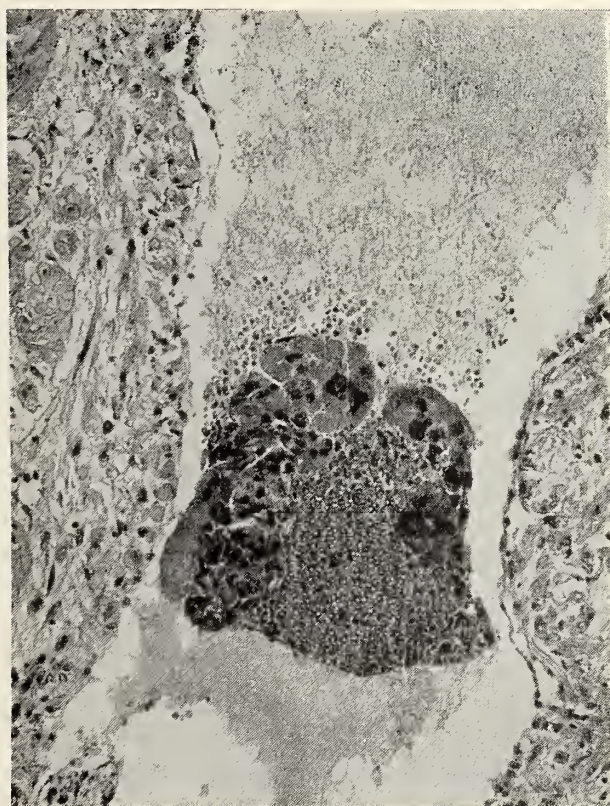


Figure 3

High power view of the tumor embolus within a vein.

blasts and syncytial cells, with evidence of vascular permeation and invasion of the tubal wall. Vacuolization of the trophoblasts was seen. No villi were identified in any of the sections.

Comment

Extrauterine choriocarcinoma may be classified according to origin as follows:¹⁰

a. Choriocarcinoma as associated with intrauterine pregnancy—the villi being transported to the tube during or subsequent to pregnancy without an initial malignant lesion.

b. Metastatic choriocarcinoma from a primary growth in the uterus.

c. Choriocarcinoma arising from chorionic cells in a teratoma.

d. Choriocarcinoma following an ectopic pregnancy.

The diagnosis of choriocarcinoma is difficult in certain instances. In a re-appraisal of 18 cases originally diagnosed and treated as chorioepithelioma, Nilehn⁷ could only confirm 11 cases. Five were classified as chorioadenoma destruens and two as syncytial endometritis. Choriocarcinoma presenting as a ruptured ectopic pregnancy is highly uncommon. Firmarola³ in 1947, studying 436 cases of ectopic gestation found no Choriocarcinoma. Heiss⁶ reviewing 540 cases from 1946 to 1953, found Choriocarcinoma in only one instance. Bobrow¹, in 905 cases of ectopic pregnancy, found that none terminated in hydatidiform mole or choriocarcinoma. Skulj⁹ claimed that prior to 1958, he had seen 60 cases of choriocarcinoma following tubal pregnancy. Hertig and Gore⁴, in a recent communication, report having seen only 6 choriocarcinomas of the tube, including this case.

Prior to the advent of methotrexate and actinomycin D, the prognosis of Choriocarcinoma was grave. Now a sustained remission can be reached in over 70% of patients.²

Summary

A patient with choriocarcinoma of the Fallopian tube, presenting with the clinical appearance of pregnancy is discussed. The course and management are outlined, and the histologic findings are illustrated in detail. A brief review of the literature affirms that this is indeed a rare condition, but one which must be considered in the differential diagnosis of an ectopic tubal pregnancy.

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Bibliography

1. Bobrow, M. L. and Bell, H. G., *Obstetrics and Gynecology* 20:500, 1962.

2. Crisp, W. E., Choriocarcinoma of the Fallopian tube coincident with a viable pregnancy. *American Journal of Obstetrics and Gynecology*, Vol. 71:2, 1956, pages 442-446.

3. Fimarola, S., *Gynecologia*, 13:49, 1947.

4. Gore, H., Personal Communication, 1968.

5. Hertig, A., Personal Communication, 1968.

6. Heiss, H. *Zentruble, Gynak*, 76:22, 1954.

7. Nilehn, B., Clinical and Histopathologic Analysis of a 20 yr. series of cases originally diagnosed as chorioepithelioma. *Acta Obstetrica et Gynecologica Scandinavica*, Vol. 41, 1962.

8. Riggs, J. A., Extrauterine Tubal Choriocarcinoma, *American Journal of Obstetrics and Gynecology*, Vol. 88:5, 1964.

9. Skulj, V., Chorioepithelioma eulopicum propter graviditatem tubariarum *Zentrallblatt Fur Gynaskologic*, 80: 1958.

10. Williams, T. J., *American Journal of Obstetrics and Gynecology*, 35:868, 1938.

A Call To Arms

Our government was founded not only to provide for the common defense but also to ensure domestic tranquillity and promote the general welfare. How well is it doing this? "The average citizen looks about him and is not satisfied with what science and engineering have given him. This because there are many things that could be done but are not being done."

"We have gone to the moon but the average citizen still can't go from one place to another safely and rapidly. Our travel methods are going to decay still further as our ground transportation from airport to city gets more complex, more dirty, more uncivilized. Many airports have themselves become overloaded, garish, trashy, littered and noisy."

"Ground transportation by train has become torture almost everywhere and no one seems to be doing much to bring it back to its former state of respect. The problem of pollution of the air, the land and our lakes and streams is getting more severe each year and solutions that are being attempted are obviously inadequate. Our garbage is not properly disposed of, old automobiles are left lying around everywhere, and beer cans and trash abound in our parks and along our highways."

"Sewage plants are overloaded and primitive and very little experimentation is going on with new systems. Our cities continue to exist with deteriorating buildings, ghetto living, overcrowding, lack of open space and conditions so miserable for some of our citizens that both mind and body are withered. What values have we set ourselves as a nation when some men must live in such primitive conditions while others cruise the universe in germfree, sterile space-cabins."

"If improvements don't come in these basic needs we will reach a time when people will demand that something be done. We are in the middle of a crises, a clear and present danger although many of us don't yet realize it as that."—*Eric A. Walker, President, Pennsylvania State University. Scientific Research*, 4, 35, March 1939.

Summer Residential Camp Accidents, Injuries and Emergencies

Harold S. Barrett, M.D.

According to the National Safety Council, accidental injury is the most important cause of death and disability in childhood.¹ Each summer a substantial number of young children are placed in residential summer camps. In Connecticut more than 230 residential camps provide camping for over 40,000 children. Systematic collection of data regarding accidents in these settings is not easily found in the scientific literature.

Accident Rates in Camping

In 1960 the Connecticut State Department of Health undertook the Family Injury Survey in Norwich, Connecticut. At the same time Charter Oak Council Boy Scouts of America opened Lake of Isles Scout Reservation located seven miles southeast of Norwich, and therefore, in practically the same climatic environment. The accident rate for boys age 10 to 14 years at home in Norwich was contrasted with the accident rate for boys in the same age group camping during the same 2 months. In general, it was found that boys at home had a higher frequency of accidents than did boys at the camp. The accident rate for boys under supervision at home (playing in playgrounds, etc.) was less than the accident rate experienced by boys not under supervision. The conclusion was drawn that camp was a safe environment because of the supervision afforded.

Meyer and others² reporting on the accidents in three separate camps, however, came up with conclusions at variance to this theory of supervision. In their study the supervisory ratio was inversely proportional to the incidence of injury with a New York Boy Scout Camp showing the lowest injury rate and the highest camper to staff ratio. The overall injury rate reported by Meyer and others has been recalculated to be 41.2 per thousand camper days of exposure. A reliable rate based on eight years of collecting data at Lake of Isles Scout Reser-

vation is 25 per thousand camper days of exposure. It is surmised now that the factor of supervision is only one item and that very likely the programming of camping has considerable influence on the accident rate. Experience with both Boy Scouts and Girl Scouts at Lake of Isles Scout Reservation indicates an average rate of 15 per thousand camper days of exposure for aquatic camps, while the regular Boy Scout camping experience rarely goes below 20 per thousand boy days of exposure although it will stay below or at a 25 per thousand boy days.

Types of Accidental Injuries

Table 1 gives calculations from three separate sources representing five camps showing the percentage distribution by type of injury for traumatic injuries. Melvin Hoffman, M.D., has kindly made the figures available for Yawgoog Scout camps. The data from Lake of Isles Scout Reservation classify lacerations only as those requiring sutures and therefore are considerably lower than the two other sources. The basic types of injury are the contusion, abrasion, and puncture wound. Differing classifications make comparison difficult.

TABLE 1

Type	TRAUMATIC INJURIES—SUMMER CAMPS—% DISTRIBUTION BY TYPE		
	Source		
	Hoffman	Meyer et al	Barrett
Contusion, abrasion, puncture	38.1	65.0	76.2
Lacerations & incised wounds	34.7	22.0	2.6
Fractures	<1.0	—	<0.1
Other	25.9	13.0	20.2

Other observations made at Lake of Isles Scout Reservation conform to the results reported by Meyer.² The basic method of injury is that of a fall or a crush injury. The incidence does not vary appreciably from season-to-season with the majority of the injuries being minor in nature. There is relatively little influence of weather on injuries and the hour of the injury is less important than the fatigue factor of the campers concerned.

DR. HAROLD S. BARRETT, member of the Consulting Staff in Medicine of the Hartford Hospital, Hartford. Deputy Commissioner, Connecticut State Department of Health and Chairman Health and Safety, Charter Oak Council, Boy Scouts of America.

Presented at a Conference on Health in Camp jointly sponsored by the Rhode Island Hospital Department of Medicine and Narragansett Council, Boy Scouts of America, May 4, 1968.

Campers and Staff

Meyer et al² called attention to a significantly higher accident rate among camp counselors than among campers. This finding has not been confirmed at Lake of Isles. The rate for counselors runs approximately 20 per 1000 days of exposure which is at the lower level for the average camper. It is felt that perhaps this lower rate is due to the junior leader and staff training week conducted before the regular camping season opens.

Tetanus occurs in persons of all ages, but particularly in the older age groups³ who may come to camp as counselors and leaders. Recent investigations of cases reported in 1965 show that essentially all cases were in persons who had had no prior tetanus immunization.³ Because of the type of injury experienced the importance of tetanus immunization for all campers and of a booster immunization within the past ten years for staff should be emphasized as a preventive measure.

Preventable Events in the Camping Experience

At Lake of Isles Scout Reservation cases seen by the medical and first aid staff are divided into three broad categories: illness, accident and environmental causes. The environmental causes are those which it is felt result primarily from the boy being in camp and are to some extent preventable. Poison ivy cases represent one type of such "accident". Each scout reporting with poison ivy is asked to list where he has been on the Reservation during the 48 hours preceding the onset. This area is checked and measures taken to destroy the ivy plant if it is within a regular troop unit site.

Snake bites are checked carefully. Parrish⁴ estimates one poisonous snake bite every three years in Rhode Island and four each year in Connecticut. The timber rattlesnake and the northern copperhead may be found in southern New England.⁵ Since Lake of Isles was opened one rattlesnake has been identified but no poisonous snake bite cases encountered. Standing orders for treatment as reviewed by Plantier⁶ and knowledge of the nearest supply of antivenin are appropriate measures designed to prevent fatalities.

Another potential danger is that of rabies. Lamson⁷ has summarized rabies in Connecticut wildlife, which would reasonably apply to adjacent Rhode Island also. There were no records of rabies in wildlife prior to 1947. Since that time a moderate number of cases have been reported in skunks, foxes and bats. There now can be little doubt but that rabies is well established in the wildlife population, primarily in the western section of Connecticut

but with some in eastern Connecticut and adjacent Rhode Island. One case of raccoon encephalitis (in the raccoon) has been identified at Lake of Isles Scout Reservation in connection with a bite suffered by a scout. This animal disease is not transmissible to humans, but the animal behavior is similar to the dumb form of rabies.

The New England Journal of Medicine⁸ in an editorial in the issue of November 23, 1967 calls attention to the fact that bats are perhaps the most dangerous sources which may be encountered in the camping situation. Rabies in squirrels and small rodents is extremely rare. As a protective measure, if any of Lake of Isles camp staff do trap small animals in advance of the camping season these animals are taken to a veterinarian and immunized, thus preventing any possible case source.

Scout survival training calls for the consuming of edible plants, roots, berries and related naturally occurring materials. It is well therefore to have at hand an identification book and to check the types of materials consumed in any case of doubt. A good illustrated reference for the southern New England area is "Common Poisonous Plants of New England"⁹ prepared by the University of Rhode Island and the Rhode Island Department of Health. Similarly some waters contain various plants, worms and other animals which may be detrimental to health. Very few of these exist in southern New England. However, when the question arises (usually as an emergency) a good reference material to have at hand is "Limnological Aspects of Recreational Lakes".¹⁰

By far the most dramatic and probably important emergencies likely to be seen in southern New England result from allergic reactions to insect stings, usually bees, wasps, yellow jackets or hornets. Parrish¹¹ has analyzed the decade experience of the 50's on a national basis and finds such fatalities account for 50% of all deaths caused by venomous animals, while snakes account for 30% by contrast. Two severe reactions, one primarily respiratory and the other recurrent angioneurotic edema principally periorbital in location have been seen at Lake of Isles Scout Reservation in 8 years of observation. Reactions are more likely in staff than in campers, and usually are most marked in the first hour following the insult.

The Need for the Camp Physician

Table 2 gives the expected frequency of events requiring medical appraisal per 1000 boy days of exposure as based on Lake of Isles experience for the past 8 years. The best prevention against illness

at camp is the screening examination. Accidents should have a followup if an identifiable hazard can be obtained when making out the accident report. It has been found helpful to make out a brief report on each case in order that future insurance claims can be validated as well as for the correction of contributory causes when possible. Lacerations usually come through the improper use of knives and the prevention therefore is that of proper programming and use. One knife, the Exacto carving knife, which is actually a bench tool, has been removed from the trading post at Lake of Isles with the consequent reduction by 50% of lacerations. The data on fractures, hospital admissions and emergency room utilization are included in this table primarily to give the physician expecting to attend camp an idea of how frequently these assisting services will be needed. Their significance basically can be interpreted in a negative kind of way: most of the accidents which happen at camp can be considered as relatively minor in terms of consequences.

TABLE 2

EXPECTED FREQUENCY OF EVENTS REQUIRING MEDICAL APPRAISAL PER 1000 BOY DAYS OF EXPOSURE

Illness	25-35
Accident	20-25
Laceration	1-2
Fracture	<0.1
Hospital Admission	<0.1
Emergency Room Utilization	0.5
Environmental Causes	15-18
Allergic Bite Reaction-Insect	4-6
Poison Ivy	10-12
Snake Bite	0.1
Animal Bites	0.1

The environmental causes already reviewed, are considered as being accidents and partially preventable events. The allergic bite reaction must be treated quite promptly. Snake bite and animal bites represent a minimal hazard but one which must be handled with dispatch and adequate treatment if and when it occurs. All in all the preparation of the staff, the supervision of the campers and good programming probably contribute more than other factors to the reduction of accidents and the prevention of unfortunate sequela from them.

Stanilonis and Meyer¹² surveyed Vermont camps in 1963, and found of 92 camps, 1/5 had no qualified person responsible for first aid, 1/2 had a nurse, and 1/6 a resident physician. Only 1 camp had no health personnel at all. The majority (84 of 92) re-

ported having physician services available, although most were not licensed in the state, and 1/3 were engaged in busy practices 10 miles or more from the camp. A sample survey of 95 camps in Connecticut done in 1967 showed 92 had a licensed registered nurse in camp and 89 a physician on call. However only 55 had standing orders issued. In neither of these surveys was the size of the camp related to the staffing pattern, which seems to be an important factor.

Summary and Conclusions

References and facts regarding summer residential camp accidents, emergencies and injuries have been reviewed and found to be sparse in number and information. With accidents such a substantial factor in childhood, and with potentially severe but preventable consequences expected in reasonable numbers the role of the medical care staffing pattern has been reviewed. The analogy to industry would lead to the conclusions that standing orders issued by an "on call" physician should always be provided, that a resident nurse was desirable in any camp larger than 50 to 100 population, and a physician in residence would be desirable in any camp over 500 and necessary in a camp population over 1000.

References

1. National Safety Council, *Accident Facts*, 1966 Edition.
2. Meyer, R. J., Kibrick, A. K., Kibrick, S., Ryan, M. P., Godbout, R., and Brown, E., *Epidemiology of Summer Camp Accidents*, Archives of Environmental Health, 7, pp. 325-330, (Sept.) 1963.
3. U. S. Department of Health, Education and Welfare, *Immunization Against Disease 1966-67*, October 1967.
4. Parrish, Henry M., *Incidence of Treated Snakebites in the United States*, Public Health Reports, 81, pp. 269-276, No. 3, 1966.
5. Parrish, Henry M., Badgley, Robin F., and Carr, Carole, *Poisonous Snake Bites in New England*, New England Journal of Medicine, 263, pp. 788-793, (Oct. 20), 1960.
6. Plantier, Henry A., *Poisonous Snakebite*, New England Journal of Medicine, 269, pp. 624-626, (Sept. 19), 1963.
7. Lamson, A., *Rabies in Connecticut Wildlife*, Connecticut Wildlife Conservation Bulletin, 11, pp. 1-6, No. 6, 1965.
8. Editorial, *Bats Batty but Rodents Rarely Rabid*, New England Journal of Medicine, 277, pp. 1147-1148, (Nov. 23), 1967.
9. *Common Poisonous Plants of New England*, Public Health Service Publication #1220, April, 1964.
10. *Limnological Aspects of Recreational Lakes*, Public Health Service Publication #1167, 1964.
11. Parrish, Henry M., *Analysis of 460 Fatalities from Venomous Animals in the United States*, American Journal of the Medical Sciences, 245, pp. 129-141, No. 2 (Feb.), 1963.
12. Stanilonis, Paul B. and Meyer, Roger J., *Health and Safety in Summer Camps*, Public Health Reports, 81, pp. 305-310, No. 4 (April), 1966.

Disseminated Intravascular Coagulation in a Newborn with Down's Syndrome

Carl Pochedly, M.D. and Gerald Ente, M.D.

It is known that infants with Down's syndrome may show transient severe myeloproliferative disorders. These disorders have included transient acute leukemia,^{1,7} labile granulopoiesis,⁸ myelofibrosis and myeloid metaplasia,⁹ polycythemia and thrombocytopenia,¹⁰ and giant platelets and thrombocytopenia.¹¹ We observed an infant who presented with evidence of severe polycythemia, marked normoblastemia, leukemoid reaction, giant platelets, congestive heart failure, and evidence of disseminated intravascular coagulation. This condition completely reverted to normal within four weeks, assisted by repeated phlebotomies.

Report of a Case

At birth this male infant had many of the stigmata of Down's syndrome, in addition to cyanosis, tachypnea, and dyspnea. His 1-minute Apgar score was 2, his 5-minute rating was 3. Blood count revealed a hemoglobin of 25 gm%, hematocrit 72%, white blood cell count 90,000/mm³ (uncorrected). The peripheral blood smear showed many normoblasts and erythroblasts, as well as many metamyelocytes and myelocytes. The liver was markedly enlarged. The possibility of congenital leukemia was suggested and the child was transferred to Meadowbrook Hospital at the age of eight hours.

History revealed that this child was born of a normal full-term pregnancy and delivery to a gravida VI, para V, 42-year-old, healthy, non-diabetic Caucasian woman. There were five living, normal siblings. The mother's hemoglobin level one week following delivery was 10 gm%. Her V.D.R.L. test was negative. The mother's blood type was A, Rh positive. The baby's blood was also type A, Rh positive. Direct Coombs' test was negative.

On initial examination (Figure 1), the baby, weighing 3742 grams, was in acute respiratory distress with cyanosis, dyspnea, retractions, and generalized pitting edema. The heart rate was 150/minute and the respiratory rate was 56/minute. The liver was palpable 6 cm. below the right costal margin. The spleen was not enlarged. No heart murmurs were heard, although the heart was enlarged by X-ray. Many stigmata of Down's syndrome were noted. Ophthalmological examination revealed normal optic fundi.

The admission hematocrit was 70% and red cell count was 5.8 million/mm³, giving a mean cell volume of 124 μ^3

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Figure 1

Photograph of patient soon after birth showing plethoric and edematous appearance of face and trunk and marked hepatomegaly. The infant required continuous oxygen at this point.

(normal for age 100-110). The white cell count was 92,000/mm³, which was corrected to 46,000/mm³ since there were 100 nucleated RBC's per 100 leucocytes on the stained blood smear. Many metamyelocytes and myelocytes were present. The nucleated erythroid cells were mainly normoblasts and late erythroblasts. Platelet count was 230,000/mm³ and many giant platelets as large as erythrocytes were seen (figure 2). The leucocyte alkaline phosphatase stain of peripheral blood showed increased numbers of positive cells, with a total score of 234 by method of Kaplow (normal 50-125). Bone marrow examination showed marked erythroid hyperplasia (90 percent), with no abnormal cells. The electro-cardiogram was within normal limits. However, X-rays of the chest showed generalized cardiomegaly. Antibiotic therapy with penicillin and kanamycin were started because of the prolonged respiratory distress. Because of the cardiomegaly, hepatomegaly, cyanosis, and edema, the baby was digitalized.

Other laboratory studies done during the first few days after admission included: Uric acid 16.5 mg%, (repeat 10.5 mg%), hemoglobin 22 gm%, hematocrit 68%, leukocyte count 41,280/mm³. Urinalysis showed a trace of albumin and specific gravity of 1.008 to 1.012. Blood urea nitrogen was 27 mg%, blood glucose was 86 mg%. Blood electrolytes were significant in that the sodium tended to be toward the lower limit of normal (132, 126, 125, and 137 mEq/liter) and the serum potassium tended to be slightly elevated (7.2, 7.7, 7.6, and 7.7

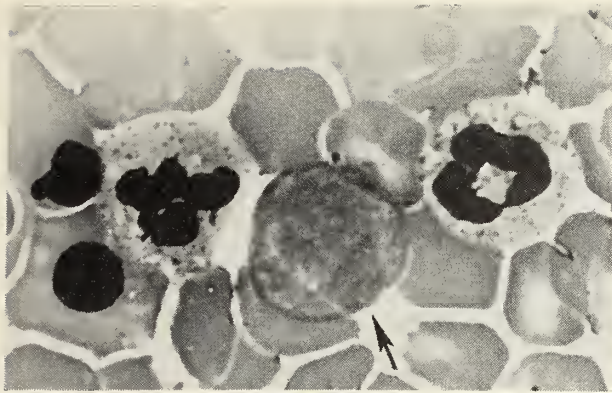


Figure 2

Photomicrograph showing one of the characteristic giant platelets found in the stained blood smear. Compare the size of the platelet with adjacent erythrocytes.

mEq/liter). Total proteins were decreased to 4.6 gm percent. The albumin was 3.4, globulins 1.2. Serum bilirubin was 1.5 mg% at 24 hours of age. Cultures of the blood, umbilicus, and nose and throat were all negative.

The child continued to show moderate to severe pitting edema on the lower extremities, over the sacrum, and on the back of the head. Venous pressure at the umbilical vein was 10 cm. of blood. The cardiorespiratory distress persisted and the patient required oxygen administration almost continuously for the first five days of life. The hematocrit remained in the range of 68 to 70%. Methemoglobin level of the blood was normal. Erythrocyte glucose-6-phosphate dehydrogenase was normal. Blood volume determination on the fourth hospital day using the ^{131}I -labeled albumin method was found to be 520 ml. (estimated normal 340 ml). Prothrombin time was 13.5 seconds, control 14 seconds. Bleeding time (Duke method) was 6 minutes, clotting time (Lee-White method) was 6 minutes, 30 seconds. However, the clot retraction after 24 hours was poor and the clot tended to be friable. The partial thromboplastin time was 81 seconds (normal 30 to 50 seconds). This prolonged partial thromboplastin time could not be corrected by addition of factor VIII, factor IX, or factor XI. The plasma fibrinogen level was found to be 100 mg% (normal 200 to 400 mg%). These findings were considered to be consistent with the occurrence of disseminated intravascular coagulation. Because of the possibility of polycythemia vera, a Fe^{59} utilization test was done. This showed only a slightly increased rate of uptake and the results did not confirm a diagnosis of polycythemia vera.

Between the fifth and tenth days of life, a total of approximately 120 ml. of blood was removed from the baby (figure 3). This represented a 20 percent decrease of blood volume. This removal of blood resulted in a profound improvement in the infant's clinical status. His breathing became easier and the cyanosis disappeared. When the child was three weeks of age, the fibrinogen level was repeated and was found to be 200 mg%, which is normal. The serum glutamic oxalacetic transaminase (SGOT) was 19 Sigma units and serum glutamic pyruvic transaminase (SGPT) was 17 Sigma units, both normal. Alkaline phosphatase was 9.5 King-Armstrong units, cholesterol was 116 mg%. Because the enlarged heart and liver suggested the possibility of storage disease, a muscle biopsy was done and reported to be normal. At the age of 17 days, the liver began to decrease in size, until at the age of four weeks, it was normal in size. The heart became smaller

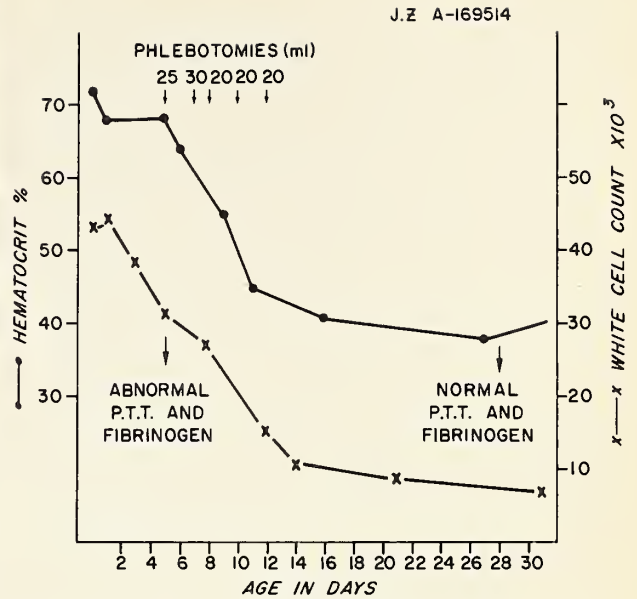


Figure 3

Graph showing the fall of the hematocrit level and white blood cell count during the first month of life. This fall was accompanied by marked clinical improvement.

in size and digitalis was discontinued. Chromosome analysis on peripheral blood lymphocytes revealed 47 XY, with trisomy on the Denver 21-22 group.

This child continued to improve and to gain weight. He was discharged in good condition at the age of 44 days. Follow-up examinations were done at two months, at six months, and 12 months of age, and the child continued to be hematologically normal.

Comment

The marked erythroid hyperplasia this infant showed could not be explained on the basis of cardiac or respiratory disease, nor on the basis of congenital polycythemia vera. The condition corrected itself following birth and improvement was hastened by withdrawal of blood. Marked erythroid hyperplasia might have been caused by placental dysfunction producing prolonged hypoxia of the baby in utero. However, the gross appearance of the placenta at the time of delivery was normal, as was the maternal course in labor. Erythroblastosis fetalis and congenital syphilis were ruled out as other possible causes.

Ross and associates⁸ introduced the term "labile granulopoiesis" which suggested an intracellular defect in regulation of leukocyte production or maturation in Down's syndrome. However, they postulated that this defect was limited to the granulocytes. Behrman and associates¹⁰ described two cases of Down's syndrome in which there were disturbances in leukopoiesis and thrombopoiesis as well. The presence of polycythemia, giant platelets,

and leukemoid reaction in our case indicated ineffective regulation in production and maturation of all three bone marrow elements. Giant platelets are seen in small premature infants, but not in full term babies except in Down's syndrome. Miller and associates¹¹ reported a case similar to Behrman's but with marked thrombocythemia. One might wonder whether these myeloproliferative disorders are related to some abnormality of chromosome 21.

Disseminated intravascular coagulation is accompanied by thrombocytopenia, but our case did not show this sign. Because of the transient polycythemia, the true platelet count was probably higher than the counts we observed and many platelets were consumed by the intravascular coagulation. Also, because of the high red cell count and macrocytosis, counting platelets was technically difficult.

The elevated serum potassium may have represented pseudohyperkalemia¹²; that is, a discrepancy between high serum and normal plasma values. This phenomenon has been described in leukemia and is associated with coagulopathy. It is thought to be due to white cell or platelet leakage of potassium during the clotting process. It is not known why this infant showed moderate hypoproteinemia.

Our case, like those previously reported, had polycythemia, leukemoid reaction, and giant platelets. But unlike past reports there was evidence of disseminated intravascular coagulation and fibrinogenopenia. Since the situation corrected itself after phlebotomy, it could not have been due to congenital deficiency of fibrinogen. Evidence of liver disease was also not present. Another possible explanation is excessive consumption of fibrinogen in the blood stream due to intravascular clotting. This intravascular clotting could have been initiated by passage of thromboplastic material, such as amniotic fluid, into the fetal circulation. This may occur with laceration of the placenta or retroplacental hematoma. Intravascular clotting is also associated with polycythemia and combined myeloproliferative disorders.¹³ In such cases there is increased red cell mass, hyperviscosity of the blood, and presence of excessive numbers of platelets. All these factors combine to facilitate sludging of blood, anoxia of the vascular walls, damage to the intima and, finally, leading to deposition of fibrin and platelets.

Another cause of consumption coagulopathy is infection. Although the present case was treated with antibiotics, all cultures were negative, erythrocyte sedimentation rate was normal, and no temperature elevations were noted. The disseminated intravascular coagulation in our case was reversible.

Multiple phlebotomies caused reduction in the viscosity of the blood which curtailed sludging of blood and the ultimate deposition of fibrin and platelets. Pulmonary microinfarcts due to disseminated intravascular coagulation may have played an important role in causing the respiratory distress and congestive heart failure seen during the first few days of life of this infant, before phlebotomies were done.

Summary

An infant with Down's syndrome (trisomy 21) presented with evidence of severe polycythemia, marked normoblastemia, leukemoid reaction, giant platelets, congestive heart failure, and evidence of disseminated intravascular coagulation. The infant's transient fibrinogenopenia was presumed to be due to excessive consumption of the fibrinogen in the blood stream by disseminated intravascular coagulation. Following phlebotomies, during which at least 20 percent of the infant's blood volume was removed, there was dramatic improvement and disappearance of the signs of congestive heart failure. Disseminated intravascular coagulation is added to the wide spectrum of findings previously reported in the myeloproliferative disorders of Down's syndrome.

Bibliography

1. Engel, R. R., Hammond, D., Eitzman, D. V., Pearson, H., and Krivit, W.: Transient congenital leukemia in seven infants with mongolism. *J. Pediat.*, 65: 303, 1964.
2. Krivit, W. and Good, R. A.: The simultaneous occurrence of leukemia and mongolism. *Amer. J. Dis. Child.* 91: 218, 1956.
3. Krivit, W. and Good, R. A.: Simultaneous occurrence of mongolism and leukemia. *Amer. J. Dis. Child.* 94: 289, 1957.
4. Lee, C. L.: Congenital leukemia associated with mongolism. *J. Pediat.* 51: 303, 1957.
5. Merrit, D. H. and Harris, J. S.: Mongolism and acute leukemia. *Amer. J. Dis. Child.* 92: 41, 1956.
6. Schunk, G. J. and Lehman, W. L.: Mongolism and congenital leukemia. *J.A.M.A.* 155: 250, 1954.
7. Storts, B. P.: Mongolism and acute leukemia; a case report. *Arizona Med.* 13: 408, 1956.
8. Ross, J. D., Moloney, W. C., and Desforges, J. F.: Ineffective regulation of granulopoiesis masquerading as congenital leukemia in a mongoloid child. *J. Pediat.* 63: 1, 1963.
9. Rosenberg, H. S. and Taylor, F. M.: The myeloproliferative syndrome in children. *J. Pediat.* 52: 407, 1958.
10. Behrman, R. E., Sigler, A. T., and Patchefsky, A. S.: Abnormal hematopoiesis in 2 of 3 siblings with mongolism. *J. Pediat.* 68: 569, 1966.
11. Miller, J., Sherrill, J. G., and Hathaway, W. E.: Thrombocythemia in the myeloproliferative disorders of Down's Syndrome. *Pediatrics* 40: 847, 1967.
12. Bronson, W. R., et al.: Pseudohyperkalemia due to release of potassium from white blood cells during clotting. *New England J. Med.* 274: 369, 1966.
13. Stefanini, M. and Dameshek, W.: The hemorrhagic disorders. Grune and Stratton, New York, 1962, pp. 347-385.

THE PRESIDENT'S PAGE

Sub-Specialization—Allied Medical Services

It is my firm belief that the availability of allied medical service personnel is a necessity and that their instruction will be on a permanent basis in the foreseeable future. Accordingly, it behooves all physicians to support such a program promptly and to the fullest extent. The plan worked successfully in the military services. There is no valid reason why it should not in civilian hospitals.

During the past decade, our physicians have faced an increasingly formidable challenge in providing medical care in their daily practice not only because there is a serious shortage of doctors trying to meet the needs of a "population explosion," but particularly because there is a critical scarcity of allied medical service personnel. Changes in nursing education, the lack of incentive and of guarantees of security as well as the cost of training prospective nurses, practical nurses, x-ray, laboratory, operating room and inhalation therapy technicians, are but a few of the hindrances to an adequate or a partial solution.

There is some hope in the efforts of various national agencies, and community and state colleges in developing acceptable programs of instruction for allied medical services personnel. These efforts are commendable, to be sure, but there are a few fundamental, serious, and perplexing questions to be answered. Until the answers are found there is some doubt that the available supply of the technologists to aid the overworked physicians will approach the need.

The first problem to consider is the cost of training. Where will the money come from? One can wonder whether the prospective student sees sufficient monetary reward in a health career to justify the outlay of personal funds for his schooling.

In addition, recruiting methods must be examined to determine their success in attracting young people into the allied medical services. The chronic shortage of these people would seem to indicate a failing in this area. And the failing may be rather in the lack of inducements for young people than in any lack of recruiting effort. There is no question in my mind that security, respect, chances for advancement and career satisfaction are important persuaders for a young man to become an O.R. Technician or a high school girl to become an I.V. Technician.

It appears that the focus of attention is on today's requirements with little thought given to the burgeoning need for allied medical service personnel in the future. As health care demands increase so will the need for allied personnel. Up to now I fear that the efforts being made are not such as to deal with this problem ten and twenty years hence.

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President, Woman's Auxiliary to the American Medical Association 1968-1969

The death of Mrs. Clifton C. Long on April 22 is a grievous loss to the AMA Woman's Auxiliary. Installed at the age of 48 as the 45th president of the 90,000-member organization, she was one of the youngest women ever to serve in this position.

Despite her illness, she carried out her official duties with remarkable determination and without complaint until only a few weeks before her death. On March 29 she returned from a trip to France as a guest of the French government and a few days later was guest speaker at the convention of the Woman's Auxiliary to the Student American Medical Association in Chicago. A day before her death, from her hospital bed she calmly made plans for the orderly transition of her presidential responsibilities to her successor.

She told a friend: "If only I could sit down with Belle (Mrs. John M. Chenault) and Margaret (Miss Wolfe, executive secretary) and talk about auxiliary just one more time . . . that would be my dearest wish."

Such courage and determination—along with an unflinching sense of humor—were outstanding characteristics of Esther Long. She was devoted to her family, to the welfare of young people and to the improvement of the quality of health of all people, but particularly rural people.

At her installation as national president last June in San Francisco, she declared: "Today young people have questions about the world, their place in it and what their future will be. We have at our disposal education programs and projects which can

help our boys and girls. This year, let's put the accent on youth."

She appointed a special committee on children and youth and in September she issued a call for auxiliaries to wage a campaign against violence in TV and movies. Wherever she went—to meetings of state auxiliaries and to speak to other organizations—she emphasized the need to do more to bring about "a brighter tomorrow" for the nation's younger generation.

In her home community of Ozark, Arkansas, Mrs. Long was the organizer of the Cub Scouts, Brownies and Girl Scouts programs. As local PTA president she worked to secure needed playground equipment, aided in sight and hearing testing of grade-school children, helped start a school lunch program for underprivileged children and was chairman of the finance committee for the high school band (even pitching in to paint the band's quarters). She was responsible for setting up the city park, for which she built two barbecue pits herself and organized the teen center.

In 1961 the governor of Arkansas appointed her to serve on the board of control of the Arkansas Training School for Girls. She took a personal interest in the girls and was responsible for many improvements in the school. In 1968 she was reappointed to a second term on the Arkansas Juvenile Training School Board.

Many of her community efforts focused on the improvement of health standards in rural Arkansas. For five years she was a judge in the unique Arkansas Rural Community Improvement program.

As rural health chairman of the AMA Woman's Auxiliary from 1962 to 1964, she was the most ardent "booster" of rural health concerns the auxiliary has ever had.

Mrs. Long's achievements were recognized in 1956 when she was voted Ozark "Citizen of the Year." For her service to rural women the *Progressive Farmer* named her "Woman of the Year" in 1964, and the Ozark Future Farmers of America awarded her the honorary degree of "Chapter Farmer" in 1965.

In her memory, the new library of the city of Ozark and a chapel at the Arkansas Training School for Girls will be named after her. The AMA Woman's Auxiliary is encouraging auxiliaries and individual auxiliary members to make memorial gifts to the American Medical Association Education and Research Foundation.

Dr. Dwight L. Wilbur, president of the American Medical Association, issued a statement to the press in which he said: "Mrs. Long typifies the finest qualities of the physician's wife, serving her husband and his profession. While her husband attended medical school at the University of Arkansas in the early 1940's, she worked as a secretary in the anatomy and chemistry departments. As wife, mother and interested partner in his profession, she has served exceptionally well ever since. Through her leadership at local, state and regional levels, it was natural that eventually she would reach the high office of national president of the Woman's Auxiliary to the American Medical Association. The American Medical Association speaks for physicians and their wives everywhere in expressing sadness at this loss and sympathy to Dr. Long and the family."

Mrs. John M. Chenault, who succeeds Mrs. Long as auxiliary president, said: "Esther Long was a true leader. Her warm personality, her down-to-earth sense of humor and her love of people made it a pleasure to work with her. She was a tremendous organizer, yet so genuinely humble I doubt she realized how skilled she really was. We loved her and we will miss her."

Surviving Mrs. Long are her husband, whom she married in 1940, three daughters—Mary (Mrs. James L. Gardner) 23, Joan, 19, and June, 16—and a son, Clifton Clay Long III, 24. Their grief is shared by her friends and co-workers, fellow physicians' wives of the Woman's Auxiliary to the AMA.

Reprinted from Md's Wife, May 1969.

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G.P.—needed for community in Litchfield County. Community has a young, growing hospital, excellent public, as well as private schools within a short distance. Community is a mixture of farming, business and industry and has many summer residents, as well as permanent residents. There is also a great need for a Pediatrician and an Ophthalmologist. For further information, contact William J. Zehring, M.D., Chairman, Medical Procurement, Candlewood Lake Road, New Milford, Connecticut.

INTERNAL MEDICINE opportunity. East Hartford General Practitioner retiring from active practice limited to Adult Medicine. Ideal central location, Hamilton equipment. Fluoroscopy.

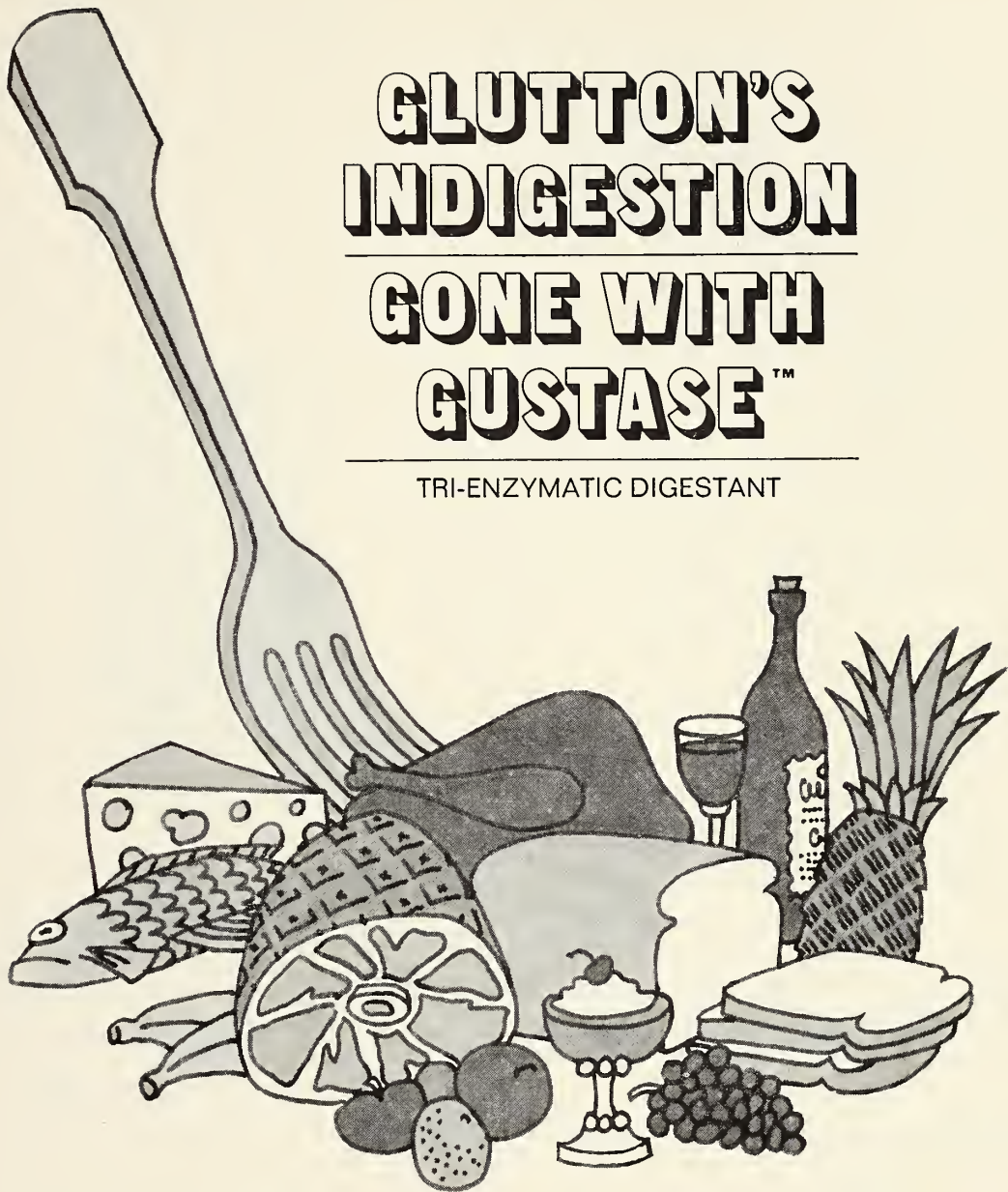
PRACTICE OPPORTUNITY FOR G.P. OR INTERNIST in upstate Connecticut at the foot of the Berkshire Hills. Office fully equipped available for rent because of death of physician. Located eight miles from excellent community hospital. Norfolk, Connecticut.

PHYSICIANS needed to practice in a rapidly expanding New England community of 45,000 (18,000 18 years and younger). Nine hospitals in immediate area. Between Springfield, Massachusetts and Hartford, Connecticut. Midway between Boston and New York. Sports, recreation, theatre, etc. are easily accessible. Contact C. S. Kissinger, Town Manager, Box 100, Enfield, Connecticut 06030.

(Continued on page 534)

GLUTTON'S INDIGESTION GONE WITH GUSTASE™

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Gustase-Plus: Gustase components plus homatropine methylbromide 2.5 mg. and phenobarbital 8 mg. (warning: may be habit forming). Side effects: Blurring of vision or dry mouth may occur. Contraindications: Glaucoma, renal disease & idiosyncrasy to phenobarbital.

Samples and literature from
Geriatric Pharmaceutical Corp.
Floral Park, New York 11001
Pioneers in Geriatric Research



(Placement Opportunities cont. from page 532)

PHYSICIAN for Emergency Room in 75 bed community hospital in northwestern Connecticut. Up to 40 hour week. Full cooperation from panel of staff physicians who cover E.R. Room for remaining time. Must be eligible for Connecticut license. Full time service approx. \$30,000 annually. Reply: Robert L. McDonald, M.D., Roxbury Falls Road, Roxbury, Connecticut 06783.

SENIOR STAFF PSYCHIATRIST, full time, residential psychiatric rehabilitation center 40 miles from New York City, in desirable living area with good schools. Non-profit Foundation oriented to intensive, individualized, eclectic psychotherapy. Large out-patient service. Salary open, dependent on experience. Benefits include major medical insurance, life insurance and pension program. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

Placement Wanted

INTERNIST—University trained, with special interest in Infectious Diseases desires private practice association with another Internist or group in Connecticut. Available on completion of military service, July, 1970. Early commitment desired.

INTERNIST—34 years of age, Board certified with National Boards desires group or associate practice in Connecticut. Military obligations completed. Available immediately. Interest in practicing general Internal Medicine.

UROLOGIST—32, married, completing residency. Board eligible, seeks interesting professional opportunity, preferably association.

OBS-GYN—30 years of age, married, Board eligible with National Boards. Wishes to practice with an associate or on a solo basis in Connecticut. Available immediately. Military obligations completed.

SURGEON—33 years of age, specialized training in vascular surgery, interested in an associate or small group type practice. Board certified with Connecticut license. Military obligations completed, available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE EXECUTIVE DIRECTOR'S OFFICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

News From Yale University School of Medicine

A \$4.5 million University Health Center, designed to serve the needs of the 30,000 people who make up the Yale community, is expected to be completed by late 1970.

The building will be part of the new Yale Health Plan (YHP), the first comprehensive, prepaid medical care program in the country to be offered to an entire university community. In addition to covering all students, it will be made available on a voluntary basis to Yale faculty members and other employees and their families.

The Yale Health Center, a six-story limestone and glass structure, will be located on the site of 17 Hillhouse Avenue. Helge Westermann-Richard Miller Associates of New York are the architects, and W. J. Megin, Inc. of Naugatuck, Conn., are the building contractors. Construction has already started.

Both the new Health Center and the YHP are expected to be in operation in a year-and-a-half, according to Joseph Axelrod, Planning Administrator for Yale's Department of University Health. While the Health Center is being designed to accommodate a total YHP membership of approximately 30,000, including families of students and employees, the program will probably start with a membership of about half that number, he said.

The new Health Center will combine office medical services and infirmary care in a single building, replacing both the old 36-bed infirmary at 276 Prospect Street and the present Department of University Health Building at 435 College Street. It will house doctors' offices, laboratories, X-ray facilities, and offices for administration and special public health programs of the department.

The infirmary, which will occupy the two top floors of the Health Center, will normally contain 70 beds and can be expanded to 140 beds to take care of the heavier winter needs of students. The infirmary will also receive observation and diagnostic admissions that do not require the full services of a hospital. The availability of infirmary care and a full range of diagnostic services in the Health Center will tend to reduce the need for hospitalization, Mr. Axelrod said, and thereby help to alleviate the shortage of hospital beds in New Haven.

At the present time, the Department of University Health offers only limited services to faculty and other employees.

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choice of a properly qualified
executor or co-executor is
especially important.*

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OBITUARY

James S. Van Leuvan, M.D.
1902-1969

Dr. James Sipple VanLeuvan, eye, ear, nose and throat physician in Meriden for the past 33 years, died unexpectedly on, June 8, 1969 at his cottage in Meriden.



Dr. VanLeuvan resided at 62 Hillcrest Terrace and maintained offices at 147 West Main Street.

Born in Yalesville May 10, 1902, he attended Lyman Hall High School. Doctor VanLeuvan graduated from Yale's Sheffield Scientific School, the former engineering department of Yale in 1924, being awarded a Bachelor of Science degree cum laude. He graduated from Yale Medical School in 1927, where he was a member of Alpha Kappa Alpha Medical Honorary Society.

He served a two year rotating internship at Hartford Hospital in 1927 and 1928. Then for three years he maintained a 15 bed hospital at Camp Crook S.D., where he was the only physician for a radius of 100 miles.

He served as a reserve officer, first lieutenant, on active duty in the U.S. Army in 1933 and 1934, stationed at Camp Spottsylvania in Virginia.

Dr. VanLeuvan then spent two years as a resident at the Baltimore, Maryland Presbyterian Eye, Ear, Nose and Throat Hospital.

He came to Meriden in 1936. His first office was located at 61 Colony Street. He was on the staff of the Meriden-Wallingford Hospital and the Veterans Memorial Hospital, currently being chief of the ear, nose and throat services at both hospitals.

For several years he has been active on the Accident Room Committee as well as the tumor clinic.

Dr. VanLeuvan served as president of the Meriden Medical Society. He was a member of the Connecticut State Medical Society and of the AMA, as well as a diplomate of the National Board of Medical Examiners.

He was also a former member and president of the Meriden Kiwanis Club. He was a member of the Home Club and Center Lodge No. 97, AF & AM.

He was a member of the First Congregational Church, United Church of Christ, where among other positions, he served six years on the Board of Deacons.

He is survived by his wife, Dorothy Dean VanLeuvan of Meriden, a daughter, a son, a grandson, a stepmother, a brother and two sisters.

John E. Hennessey, M.D.

In Memoriam

Buxton, Charles Lee, New Haven, Columbia University 1932. Professor of Obstetrics and Gynecology at the Yale School of Medicine and former chairman of the department. Dr. Buxton was born in Superior, Wisc., and attended Lawrenceville School, Lawrenceville, N.J., and Princeton University. He interned at Mary Imogene Bassett Hospital, Cooperstown, N.Y., spent a year doing endocrinology research at Harvard Medical School, and joined New York's Sloane Hospital for Women for a series of internships and residencies in pathology, obstetrics and gynecology. He became an assistant attending, later associate, in obstetrics and gynecology and in 1947 was named chief of the Sloane Sterility and Endocrine Clinic. In the years 1938-51 Dr. Buxton rose from assistant professor to full professor on the Columbia University medical faculty. He joined the Yale faculty in 1954 and later was appointed Chairman of the Yale Department of Obstetrics and Gynecology. He resigned as chairman in 1966 for reasons of health. Dr. Buxton was one of the world's leading authorities on the problems of fertility, sterility and family planning. He was one of the important figures in the landmark Supreme Court decision of 1965 which resulted in the overturn of Connecticut's birth control law. For years he served as medical director of the Planned Parenthood League. He was a member of the American Gynecology Society, American Academy

of Obstetrics and Gynecology, American Fertility Society, Society of Gynecology and Investigation, American College of Obstetrics and Gynecology, American Medical Association, Connecticut State Medical Society and the New Haven County Medical Association. Dr. Buxton died July 7 at the age of 64.

Hill, E. Roland, Mystic, Jefferson 1924. Dr. Hill was a general practitioner in the New London area for many years. He served in the Navy Reserves from 1917-1919. Dr. Hill was on the staff of the Lawrence and Memorial Hospital. He was a member of the American Medical Association, Connecticut State Medical Society and the New London County Medical Association. Dr. Hill died April 30 at the age of 72.

MEETINGS

GENERAL

September 24 5:00 P.M.
177th Semi-Annual Meeting of the Hartford County Medical Association
Hartford Hilton Hotel, Hartford
Speaker: Victor R. Fuchs, Vice President in Charge of Research, National Bureau of Economic Research. Subject, "The Economists Rx for the Medical Care Industry."

October 1
177th Semi-Annual Meeting of the Fairfield County Medical Association
Greenwich Country Club
October 23
186th Semi-Annual Meeting, New Haven County Medical Association
Waverly Inn, Cheshire
Business Meeting 3:00 P.M.; Social Hour and Dinner to follow

MEDICINE

September 7-12
Second Conference on Experimental Medicine and Surgery in Primates
Auditorium, Hunter College-Bellevue Department of Nursing Education, 440 East 26th Street, New York, N.Y.
Sponsored by the New York University School of Medicine.
Registration fee \$25. Fee waived for graduate and undergraduate students and house officers submitting a letter from their academic sponsor.

Contact J. Moor-Jankowski, M.D., Conference Co-Chairman, New York University Medical Center, 550 First Avenue, New York, N.Y.

Peter Bent Brigham Postgraduate Medical Series
September 12 8:30 A.M.-5:30 P.M.

"Renal Failure: Concepts in Current Management"
John Merrill, M.D., Director, Cardiorenal Section, Peter Bent Brigham Hospital

The series is aimed at the practicing physician, held the second Friday of each month September-May. Attendance limited to 100. Fee is \$30 per course or \$250 per series, lunch included.

Contact David P. Lauler, M.D., Peter Bent Brigham Hospital, Boston, Mass.

September 26-27

Regional Meeting (New England, Canada) of the American College of Physicians

Mary S. Harkness Auditorium, Yale Medical School

SURGERY

September 8-November 22

12th Series of Ophthalmology Postgraduate Courses
Postgraduate Institute of New York Eye and Ear Infirmary, 310 East 14th Street, New York City.

At the conclusion of the regular series, there will be a one week postgraduate course designed as a review in basic sciences in ophthalmology. Write Jane Stark, Registrar, at the Institute.

January 15, 1970

Conference, Connecticut Chapter of the American College of Surgeons

Park Plaza Hotel, New Haven

Contact: Francis M. Hall, M.D., 140 Woodland Street, Hartford

National Academy Of Medicine Founding Within Year

A National Academy of Medicine will probably be established within the next year or so according to Presidential Advisor, James A. Shannon.

The proposed academy "should tap leadership in medical schools, hospitals and private practice in order to collect information on which to base mature judgments concerning the place of medicine in society today and the distribution of government funds for research, education and service in the health fields."

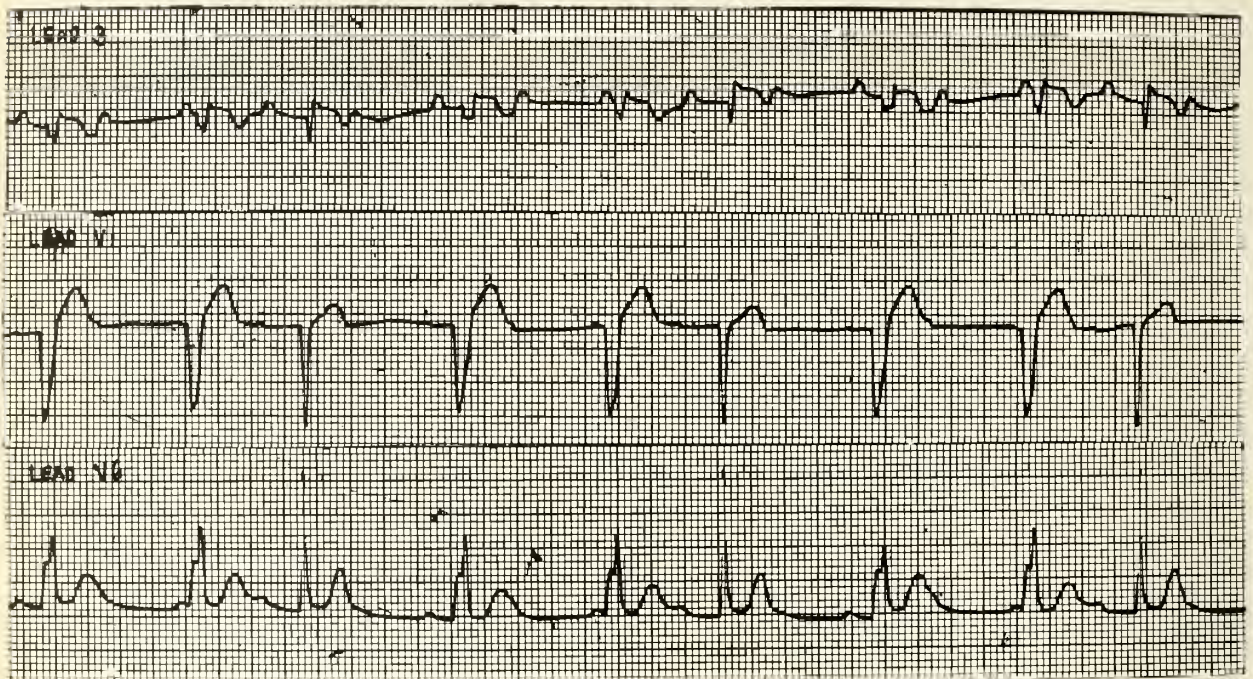
There will be a group of about fifty charter members. The new academy's relationship to the other Academies of Sciences and Engineering is being discussed. There seems at present no opposition to the establishment of such an Academy.—L.H.N. *JAMA*, 208: 952, May 12, 1969.

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Director, Dept. of Electracardiography
Memorial Unit, Yale-New Haven Hospital

E.R. a 55 year old white male, was admitted to Yale New Haven Hospital on 2-3-69 because of severe chest pain. An electrocardiogram revealed evidence of recent infarction of the inferior wall. The rhythm was sinus with an occasional VPC. First degree AV block was present with PR interval of 0.22 sec. On the 3rd hospital day he was noted to have the following rhythm disturbance:



Which of the following is the most likely arrhythmia present?

1. Sinus Bradycardia with premature atrial beats as every 3rd beat.
2. Sinus Arrhythmia with Intermittent Left Bundle Branch Block.
3. Sinus Tachycardia with 2nd degree AV block with alternating 2:1 and 3:2 Wenkebach periods.
4. AV Dissociation with Sinus capture beats
5. Sinus Arrhythmia with Intermittent WPW phenomenon.

The arrhythmia present is AV dissociation with periodic capture of the ventricles by a sinus impulse. The atria are under sinus control at a rate of 120/min. The ventricles are under control of an AV junctional pacemaker beating at a rate of 64/min. The QRS complexes elicited by the AV junctional impulse exhibit aberrant I-V conduction and increased I-V conduction time. Following every two AV junctional beats there occurs capture of the ventricles by a sinus conducted impulse. The PR interval of these beats is always approximately 0.27 sec., and the QRS complexes are of normal duration. The reason that the AV junctional pacemaker

assumes control of the ventricles is that 2:1 AV block is present. Although the sinus is beating at 120/min., the effective sinus rate is only 60/min. because of the presence of 2:1 AV block. Since the escape AV junctional pacemaker has a faster discharge rate (65/min.) it assumes control of the ventricles. Sinus capture of the ventricles occurs whenever a sinus beat arrives at the AV junction sufficiently late enough after an AV junctional beat so as to find the AV junction recovered sufficiently to transmit the sinus impulse. Since the effective sinus rate and the AV junctional escape rate in our pa-

tient are not too dissimilar, this permits sinus capture of the ventricles to occur as every third beat.

AV dissociation with or without sinus capture is commonly seen as a rhythm disturbance in patients with myocardial infarction, particularly when the infarction is of the inferior wall. In most patients the blood supply to the sinus node and to the AV node comes from the right coronary artery. Impaired blood supply to these nodes may impair impulse formation or impulse conduction and thus create the need for an escape rhythm to assume control of the ventricles.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

LOUIS H. NAHUM, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511



*Clues to
PVD*

The heavy smoker with vasospasm

He may be comparatively young or approaching middle age. Typically, he is a heavy cigarette smoker—a pack or more a day for a number of years. Whether smoking is a causative or an important exacerbating factor in peripheral vascular disease is still under discussion. But the vasoconstrictive effects of nicotine are firmly supported by a substantial body of laboratory and clinical evidence, and the close association is now generally accepted.

Thus, a history of heavy smoking coupled with vasospasm may serve as warning signals to the physician. When a diagnosis is established, therapeutic measures are directed toward increasing the local circulation, and appropriate management of the patient's general medical needs should be instituted. These include the important safeguards of keeping warm and refraining from smoking.

Letters To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Dr. Nahum:

I have just finished reading your article "Medical Dogma: The Duration of Pregnancy" on page 228 of the April issue of *Connecticut Medicine*.

I am in agreement with the first sentence of your last paragraph when you state "the old method of calculation of pregnancy may not have contributed unnecessarily of interfering 'with the very wonderful natural processes of childbirth'." However, I am not in agreement with your first sentence of the second paragraph. In this you state that it is now accepted that ovulation most frequently happens on about the 14th. day of the menstrual cycle. Herein lies the crux of this whole problem of determining the expected date of confinement.

What should have been written is that ovulation occurs usually 14 days *before* the next menstrual period and not 14 days after the start of the menstrual period. If my particular interpretation is correct, then the significant thing in determining the expected date of confinement is not by adding seven, eight, nine, or ten days to try to come out to the 41st. week but to determine first the length of the girl's menstrual cycle. For example, a girl with a 28 day cycle that is always regular probably should follow the old rule of adding seven days and subtracting three months. However, the girl who has a 35 day cycle should not add seven days and subtract three months, but should add 14 days and subtract three months. I believe if you took your first sentence of the fourth paragraph which states the majority of normal births, that is 57 per cent take place in the 41st. and 42nd. week would also show that about 57 per cent of all menstrual cycles are in excess of 28 days duration also. It has always been interesting to me that when I give lectures before girl's schools and ask them, how many

girls have a 28 day cycle that this number always turns out to be in the minority.

As an obstetrician who tries hard to try to reach a satisfactory date for the patient, I find that if the rule of using a date of ovulation as being 14 days before the end of a menstrual period and not after a menstrual period that one can come much closer to a correct expected date of confinement. For example, a girl who has a period every forty days would ovulate approximately on day 26 of her menstrual cycle and this particular girl should add 19 days to the day of her last menstrual period and subtract three months. I am now becoming repetitious so I think it is time to stop this letter.

I do enjoy reading your critique every month and I do find them most scholarly.

Most cordially,

J. Brooks Hoffman, M.D.

Greenwich, Conn.

Dear Dr. Nahum:

Doctors Hess and Hoffman are correct in pointing out that the statement "It is now accepted that ovulation most frequently happens on or about the 14th. day of the menstrual cycle," which appeared in the editorial "Medical Dogma: The Duration of Pregnancy" (*Connecticut Medicine*, April 1969) is in error. The two week interval between ovulation and menses is the more rigidly controlled factor of the menstrual cycle. The preovulatory phase accounts for the variability in total cycle length and leads to the uncertainty in the EDC calculations cited in your editorial.

Even the postovulatory phase displays some variation in duration. Calculating from the serum LH surge or the thermal nadir to the first day of menses reveals intervals of 11-18 days. This irregularity is a common finding during the pharmacologic induction of human ovulation. Currently we do not define a cycle as ovulatory if the temperature elevation is less than eleven days long. Elevation beyond twenty days implies the presence of early pregnancy.

One further point must be made in this discussion. Antenatal estimates of the biochemical maturity and well being of the fetus are now available (urinary estriols, amniotic fluid estriols, bilirubin, creatinine, etc.) These have been applied to the management of anticipated or actual high risk preg-

nancies with resulting improved survival and quality of neonates. As more obstetricians turn to these measures, their clinical concern over the imprecision of EDC as presently calculated will diminish.

Sincerely,
Nathan Kase, M.D.
Associate Professor
Department of Obstetrics
and Gynecology

Yale University
School of Medicine

Dear Dr. Nahum:

Thank you for permitting me to see the interesting letter from Dr. J. Brooks Hoffman.

In general, I believe it is widely accepted that ovulation normally occurs 14 days before the next menstrual period. The explanation for this is based customarily on the theory that ovulation controls the physiologic mechanism involved in the onset of endometrial desquamation and bleeding. This does not account for "anovulatory bleeding" and the "menstruation-like" bleeding which commonly occurs with the use of the "pill" and with other types of administration of endocrine therapy.

My thought is that it might be interesting to get the point of view of Dr. Kase and Dr. Glass (Yale School of Medicine, OB-GYN Department) who have been conducting investigations in inducing ovulation and may have secured objective data on the time relationship between "ovulation and menstruation."

Cordially yours,
Orvan W. Hess, M.D.
Medical Director

State Welfare Department
State of Connecticut, Hartford

To the Editor:

The editorial on "The Problems of the Volunteers in Medical Research" which appeared in the March issue of *Connecticut Medicine* brings to mind another group from which such volunteers might well be recruited.

Since it is now legal in a number of states for an individual to donate his body to a medical school for anatomical studies, many of all ages have taken advantage of the opportunity. Here each volunteer has demonstrated his "altruism" in wishing to take part in forwarding medical knowledge. Some of these may be suffering from conditions being studied intensively at the school to which the body is

to be brought and they would probably be glad to participate in the studies. Many of them at all ages may be well and willing to serve as controls in other studies. Some might be glad to serve in studies involving inconvenience, discomfort and "risk."

Two exceptional advantages existing in this group should be pointed out. Their names are on record at the school and their bodies will be delivered to the school for prompt post-mortem preparation so that pathological studies will be available.

In my own practice, two volunteers among my younger patients have expressed an interest in taking part in such studies so the idea is not "far fetched."

Certainly, in addition to allowing these individuals to serve as anatomical material, the possibility of making further use of the good will of the group should be explored.

Maurice T. Root, M.D.
West Hartford, Conn.

Doctor's Office

William B. Henry, M.D., announces his association with James Walker, M.D. and Christopher F. O'Connor, M.D. for the practice of pediatrics at 2900 Main Street, Glastonbury.

David H. Hild, M.D., announces the opening of an office for the practice of internal medicine and hematology at 85 Jefferson Street, Hartford.

Herbert R. Kuhn, M.D. and Frank G. Marx, M.D., announce the association of Gilles A. Marchand, M.D. for the practice of gynecology and obstetrics at 425 Montauk Avenue, New London and 165 Broad Street, Groton.

Russell A. Lobb, M.D., announces the relocation of his office for the general practice of medicine to 1 Essex Street, Deep River.

Walter E. Pleban, M.D., announces the opening of an office for the practice of general surgery and gynecology at 3589 Main Street, Stratford.

Daniel Purcell, M.D., announces the opening of an office for the practice of general medicine at 342 Main Street, Manchester.

Thomas Eric Walshe, M.D., announces the relocation of his office for the general practice of medicine to 509 Wolcott Road, Wolcott.

LABORATORY NOTES

Disorders of Lipid Metabolism

Background

Fredrickson and Levy¹ at the NIH have greatly expanded our understanding of lipid metabolism disorders by creating 5 reasonably well defined categories of disturbance. These bear a convincing correlation² with some clinical disturbances involving lipids, glucose metabolism and vascular disease. The categories are: (N-normal, E = elevated, EE = markedly elevated, pattern = electrophoresis)

Type I

Hyperchylomicronemia

Cholesterol E, triglycerides EE

Plasma: creamy, infranate clear

Pattern: fasting chylomicron fraction present

Glucose Tolerance: usually normal

Type II

Hyper-beta Lipoproteinemia

Cholesterol EE, triglycerides N or E

Plasma: clear

Pattern: increased beta band

Glucose Tolerance: usually normal

Type III

Hyperlipoproteinemia-broad beta disease

Cholesterol EE, triglycerides E

Plasma: clear, cloudy or milky

Pattern: broad beta band

Glucose Tolerance: abnormal in 40% of cases

Type IV

Endogenous Hyperlipemia

Cholesterol N or E, triglycerides EE

Plasma: clear, cloudy or milky

Pattern: increased prebeta band

Glucose Tolerance: abnormal in 70% of cases

Type V

Mixed Hyperlipemia

Cholesterol E, triglycerides EE

Plasma: creamy, infranate turbid

Pattern: fasting chylomicron band, increased pre-beta band

Glucose Tolerance: usually abnormal

Instructions

1. Patient should be on a normal diet at a stable weight for at least 1 week.

2. Blood is drawn after 12-16 hour fast.

Lab. Procedure

We will note the plasma appearance, cholesterol level and appearance of the lipoprotein electro-

phoretogram. The pathologists interpretation will comment on the need for actual triglyceride level which will be infrequent. We are doing the electrophoresis ourselves by the method of Noble and the separations are excellent, far better than those done by the outside laboratories to which we had been referring them. The cholesterols by the direct method of Kim and Goldberg are more precise than the usual automated techniques.

Charge for cholesterol and lipoprotein will be \$14.50.

Notes from Dr. Lawrence Freedman (5/8/69)

1. Several hours after ingestion of aspirin there are many WBC in the urine for 2-4 hours.

2. Renal papillary necrosis occurs after ingestion of large amounts of analgesics, particularly phenacetin, and with chronic alcoholism. It may be unilateral.

Roy N. Barnett, M.D.

1. Levy, R. I. and Fredrickson, D.S. A.J. Cardiol. 22, 576, Oct. 1968.

2. Wessler, S. and Avioli, L. A. JAMA 207, 929, Feb. 3, 1969.

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NEW BOOKS IN REVIEW

PRACTICAL PSYCHIATRY FOR THE INTERNIST.

Edited by Douglas Goldman, M.D. and George A. Ulett, M.D., Ph.D. The C. V. Mosby Company, St. Louis, 1968. 168 pp. \$9.85.

Reviewed by: LOUIS H. NAHUM

All aspects of the treatment of illness have same psychiatric implications. Doctors have always recognized that some part of the treatment of his patient must be directed specifically toward emotional and psychologic components of the illness. But he also recognizes that there are mental illnesses as well as psychologic components of physical illness. There are psychiatric skills which are necessary also since the internist can if he is acquainted with the dynamics of psychiatric illness handle many of them well and become in fact the major treatment link between the public psychiatric facility and the community.

Today the physician will discuss with the family the nature of the mental illness, alternative methods of treatment, possibility of home treatment. This, of course, will require increased surveillance and tolerance on the part of the family which could be promoted by the knowledgeable physician and in some instances bring about the best hope for ultimate recovery. In this book by Dr. Goodman and Dr. Ulett we have a worthwhile contribution on the subject of psychiatry for the non-psychiatric physician. It presents clearly the basic principles of personality development and personality dysfunction.

The book begins with a chapter on developmental stages of dynamic psychiatry and is filled with interesting clinical case reports which are used as a springboard for discussion of psychiatric problems seen in general medical practice, surgery and specialties and the psychiatric treatment measures suitable for use by the internist.

Two chapters of treatment measures, one on hypnosis, and one on community mental health are well written. There is a chapter on the physician himself, since he should be aware of his own emotional and psychologic functions, because of the likelihood that he will become involved in the therapeutic interchange. There is a reading list presumably to suitably extend the purposes of the volume. Interestingly Sigmund Freud is not on the list and on page 63 "subconscious" is employed, a word hardly belonging in a psychiatric treatise even though it fills much literature and the lay press.

There is no doubt that the future practice of medicine will require familiarity at the working level with psychologic and emotional aspects of general illness and with mental illness also particularly with practical therapy and application of clinical and physiologic knowledge of psychopharmacology. This volume will help provide an introduction to this working knowledge.

INTRODUCTION TO MEDICAL SCIENCE. Edited by Clara Gene Young and James D. Barger, M.D., F.A.C.P. The C. V. Mosby Company, St. Louis, 1969. 295 pp. Illustrated. \$7.95.

Reviewed by: LOUIS H. NAHUM

The first author is technical editor and writer and the second is a physician and pathologist at Sunrise Medical Center, Las Vegas.

It is intended for those who work alongside the physician, the paramedical personnel. They are the ones carrying out the doctor's order and if they had some knowledge of the patient's disease and why certain diagnostic tests and procedures are ordered it might lead them to a better understanding of the sick person.

Mechanical performance of a duty cannot lead to real enjoyment of it. This book will lead to further investigation of the disease understudy and can correct error and help to correlate observations with their explanation.

It is a sort of continuing education which now all agree will become a part of modern medical training whether it is on the wards or in special care units.

Almost all of medicine is covered in it. As an aid in understanding the principles of disease mechanisms the authors have introduced a step by step progressive method for teaching of the material presented. It is a type of programmed instruction in which the reader becomes an active participant by responding to certain questions at each learning step.

This permits individualization of instruction. The steps are especially valuable because they make it possible for the reader to recognize the points that are important to him in understanding disease, its origin, its manifestations, its diagnosis and therapy.

The steps can also serve as a guide to an instructor in completing similar steps to augment his teaching methods.

The book is really a must for nurses, medical technologists, social workers and medical supervisory personnel as well as their instructors, and also biologists and students of biology.

CYSTIC FIBROSIS. Ciba Foundation Study Group No. 32. Edited by Ruth Porter and Maeve O'Connor. Little, Brown and Company, Boston, 1968. 150 pp. with 8 illustrations. \$3.95.

Reviewed by: DAVID B. HICKOX

This small book, which is written as a symposium, represents an effort to assemble current thoughts on the pathogenesis of Cystic Fibrosis into one volume. The participants are primarily from England and Europe with the notable exceptions of Guilio Barbero and W. S. Chernick from this country. Much of the research in C/F has had to do with the nature of the various exocrine secretions produced in patients with this disease as well as the autonomic and pharmacologic influences on glandular secretions. This work is outlined in some detail followed by some rather searching questions and discussions after each topic has been presented. I rather hoped that some more space would be devoted to the interesting work of Alec Spock at Duke University who seems to have found clues to discovering carriers of C/F. He also has some evidence that plasma humoral substances are involved in this disease rather than changes in gland structure or autonomic balance. It should come as no revelation to most readers that there is very little known of the mechanisms of this disease. The pieces of the puzzle presented here represent years of laboratory study and thought, but they do not fit together in a way that is going to give the practicing physician a unifying concept of the pathogenesis of C/F. This is not the fault of the symposium participants or the editors. It is simply the result of our current level of knowledge.

RENAL DISEASE IN CHILDHOOD. Edited by John A. James. The C. V. Mosby Company, St. Louis, 1968. 371 pp. with 104 illustrations. \$18.50.

Reviewed by: LEONARD S. KRASSNER

There has been a genuine need for a book dealing with the specific problems involved in caring for children with renal disease. Dr. James has attempted to fill this need by single handedly tackling this complex problem in a book conceived as a "concise practical guide for pediatricians, urologists, general practitioners and residents in training."

Written within these limits, the book is handicapped by the necessity of being arbitrary in a field where speculation and hypothesis are everyday realities, and by being brief when only a more extended discussion can provide a student with the insight necessary for the practical application of our present knowledge. Once having accepted this frame of reference one can then attempt to deal with the content of this volume.

The early chapters of the book on anatomy, physiology and embryology are brief summaries which offer no new approaches in concept or teaching. Their inclusion seems almost perfunctory.

The sections on the significant differences in renal function in the infant and child are unfortunately quite brief. This would seem to be a mistake in a book concerned with pediatric renal disease since this particular aspect must be a major justification for another book on kidney disease.

The strongest chapters in the book are those dealing with the clinical problems of nephritis, nephrosis and renal failure. The author is a clinician of some experience, and these areas are covered in a concise and practical manner. To use this book as a guide in treatment, however, necessitates more liberal use of references to the bibliography so that the reader may document facts and broaden his knowledge on specific aspects.

A final observation one comes to after reading this volume is how hard it is for one man to be able to write on all aspects of renal disease by himself. Dr. James is quite honest and frequently mentions well-accepted concepts described in the literature with which he has no experience, i.e. use of fluoroscopy and the image intensifier during renal biopsy. It would indicate that the days of the single author writing on a broad, rapidly changing field must indeed be numbered.

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Controversy In Obstetrics And Gynecology. Edited by Duncan E. Reid, M.D. and T. C. Barton, M.D. with 60 eminent contributors. W. B. Saunders Company, Philadelphia and London, 1969. 414 pp. Illustrated. \$15.50.

Genetics And Counseling In Medical Practice. Edited by Leonard E. Reisman, M.D. and Adam P. Matheny, Jr., Ph.D. The C. V. Mosby Company, St. Louis, 1969. 215 pp. with 86 illustrations. \$12.75.

Organization And Administration Of Health Care. Edited by Richard L. Durbin and W. Herbert Springall. The C. V. Mosby Company, St. Louis, 1969. 248 pp with 51 illustrations. \$9.85.

Hypertension, Volume XVII. Experimental Hypertension. Edited by Patrick J. Mulrow, M.D. Proceedings of the Council for High Blood Pressure Research, American Heart Association, Cleveland, October 11 and 12, 1968. The American Heart Association, Inc., New York, 1969. 148 pp. \$4.00.

Cardiovascular Surgery 1968. American Heart Association Monograph Number 24. Edited by C. Frederick Kittle, M.D. The American Heart Association, Inc., New York, 1969. 274 pp. \$4.00.

The Role Of Learning In Psychotherapy. A Ciba Foundation Symposium. Edited by Ruth Porter. Little, Brown and Company, Boston, 1969. 340 pp. with 30 illustrations. \$12.00.

Adrenergic Neurotransmission. Ciba Foundation Study Group No. 33. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Little, Brown and Company, Boston, 1969. 123 pp. with 12 illustrations. \$4.50.

Internal Medicine In World War II. Volume III. Infectious Diseases And General Medicine. Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Editor in Chief, Colonel Robert S. Anderson, MC, USA. Editor for Internal Medicine, W. Paul Havens, Jr., M.D. Office Of The Surgeon General, Department Of The Army, Washington, D.C., 1968. This 712 page volume with 123 illustrations, 6 plates, 8 charts, 105 tables, and a comprehensive index is available for purchase at \$8.25 per copy from the Superintendent of Documents, Government Printing Office, Washington, D.C., 20402.

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Immunosuppression with azathioprine, adrenal steroids, and antilymphocytic globulin has not been as successful in combatting rejection over the long term as earlier experience indicated.—L.H.N. *New Eng. J. Med.*, 280: 1079, May 15, 1969.

Some Tranquilizers And Antidepressants May Lead To Heart Abnormalities

Dr. Carl S. Alexander found three patients with disturbed heart rhythm, four with enlarged hearts and two had suffered heart attacks. The drugs used by these patients were phenothiazine and imipramine over a period of years. He advises that electrocardiograms be taken every three to six months on such patients.—L.H.N. *Heart Research Newsletter*, 13: 4, 1969.

Elevated Cholesterol May Increase Lung Cancer Risk In Smokers

Dr. Jeremiah Stamler of Chicago analyzed 876 cigarette smokers who were 40-59 in 1958. There were 354 men with cholesterol levels less than 225 mg. per 100 cc.'s of blood, 342 in the 225-274 range and 180 above 275. Those with the highest levels showed a 9 year cancer mortality rate that was more than 7 times greater than that of the low group. The middle group had a death rate that was more than 3 times higher than the low group.

Thus already widely implicated as a risk factor in heart attacks, elevated levels of blood cholesterol seem also to be associated with increased risk of lung cancer in cigarette smokers.—L.H.N. *Heart Research Newsletter*, 13: No. 4, page 7, 1969.

The Food And Drug Administrations Action To End The Marketing Of Seventy-Eight Antibiotic-Containing Drug Products

This decision by the FDA was based on recommendations of the National Academy of Sciences—National Research Council which is evaluating the effectiveness of about 3,600 new drugs marketed from 1938-1962.

The seventy-eight products named were found ineffective as "fixed combinations" for claims made in their labeling. This, of course, does not mean that either the antibiotic or other active ingredients of the product are ineffective when used alone.

The majority of the seventy-eight products tested are antibiotic-sulpha combinations in tablet, capsule or liquid forms. Also included are sixteen penicillin-streptomycin combinations that are given by injection. In addition to many other antibiotic combinations are those that contain analgesics, vitamins or other ingredients.—L.H.N. *Bulletin of the American College of Physicians*, 10: 226, May 1969.

Development Of Reticulum Cell Sarcoma At the Site Of Antilymphocyte Globulin Injection In A Patient With Renal Transplant

Dr. S. D. Deedhar and his colleagues report a case who developed a sarcoma at the site of antilymphocyte globulin injection given to prevent rejection of a renal transplant. They believe this to be a cause and effect relationship.

The possible mechanisms involved in such malignant transformation are considered likewise, the true frequency and gravity of such neoplastic complications in transplantation are not entirely clear. However the possible etiologic role of ALG in such malignant lymphoid tumors becomes an important consideration in view of the widespread use of this agent in clinical transplantation.—L.H.N. *New England Jr. Medicine*, 280: 1104, May 15, 1969.

Politics And Pollution: The Taconite Affair

One of the harsh realities of the struggle against air and water pollution is that companies which are big polluters also meet big payrolls and have political punch. A recent story about the "taconite affair" in this newspaper provides the latest proof of this.

The Reserve Mining Company of Duluth, Minnesota, a jointly owned subsidiary of the Republic Steel Corporation and the Armco Steel Corporation, dumps 60,000 tons a day of ore waste from its taconite mining operations into Lake Superior. Last year, a Federal interagency task force investigated and prepared a report showing that Reserve is the only one of a half-dozen mining companies depositing its waste in the lake rather than on shore and that on-shore disposal could be arranged at moderate cost. The task force recommended that the dumping be stopped.

No action was taken on the report. Representative John A. Blatnik of Minnesota, a senior member of the House Public Works Committee, whose district includes Duluth, denies that he intervened on behalf of the company. But there is no doubt that there were, in the words of a former Department of Interior official, "tremendous pressures" to disown the report. The Water Pollution Control Administration next conducted its own survey and initiated public hearings which are now under way. But it merely proposes to keep the discharge of ore waste "under continuing surveillance." This is not good enough.

Lake Superior is still relatively clean. If it is to avoid dreadful pollution which has nearly killed Lake Erie as a living body of water, prompt action has to be taken to halt the reckless dumping of wastes. No short-term benefit to any region or company can justify the destruction of the nation's water resources.—*The New York Times*, May 16, 1969.

Davy Jone's Dustbin

After the death of 6,000 sheep in Skull Valley, Utah by poisoning with nerve gas, people are up in arms about a decision by the military to dump 27,000 tons of nerve gas in the Atlantic. There is chance of accidental spilling, risk of polluting the sea and maritime life around it. People demand

that the U.S. Army should provide the information to permit a reliable estimate as to how long the potential hazard will endure. We are not told what the chemicals are.

Many assumptions underlie the conclusion that it is a safe venture. What if deep sea currents alter their course. Overconfidence is not merely misleading but may be damaging and is another illustration that public authorities for the sake of convenience are prepared to take all kinds of risks.

It is ironic that this should happen when we are engaged in negotiations to design a treaty for governing the use made of the sea bed. It is even more unsettling to think that the government has accumulated and paid for such vast stores of dangerous chemicals that were not needed in the first place and must now be destroyed.—L.H.N. *Nature*, 222: 619, May 17, 1969.

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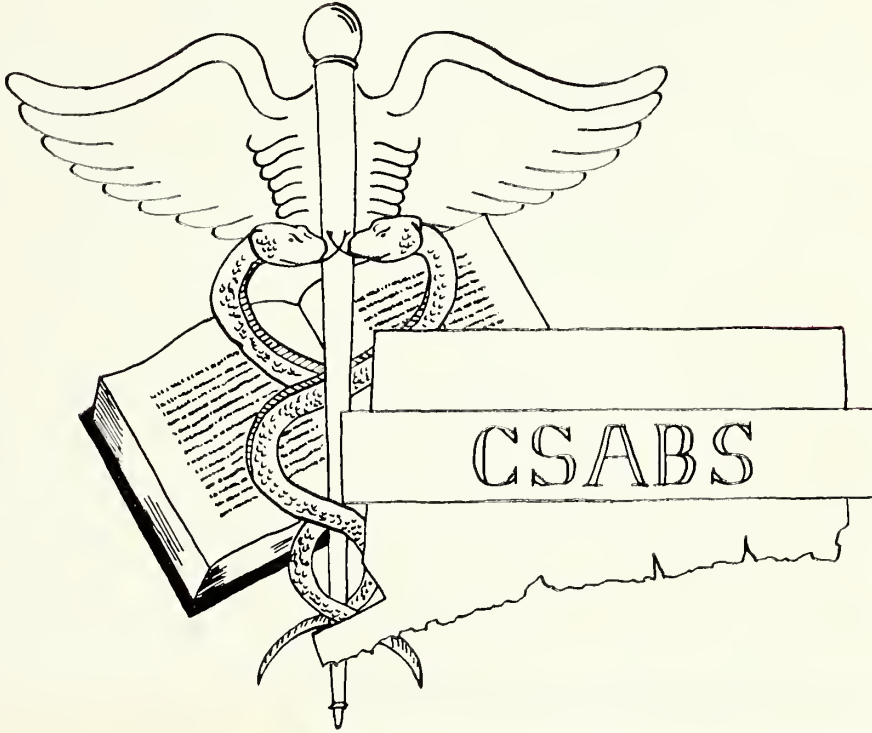


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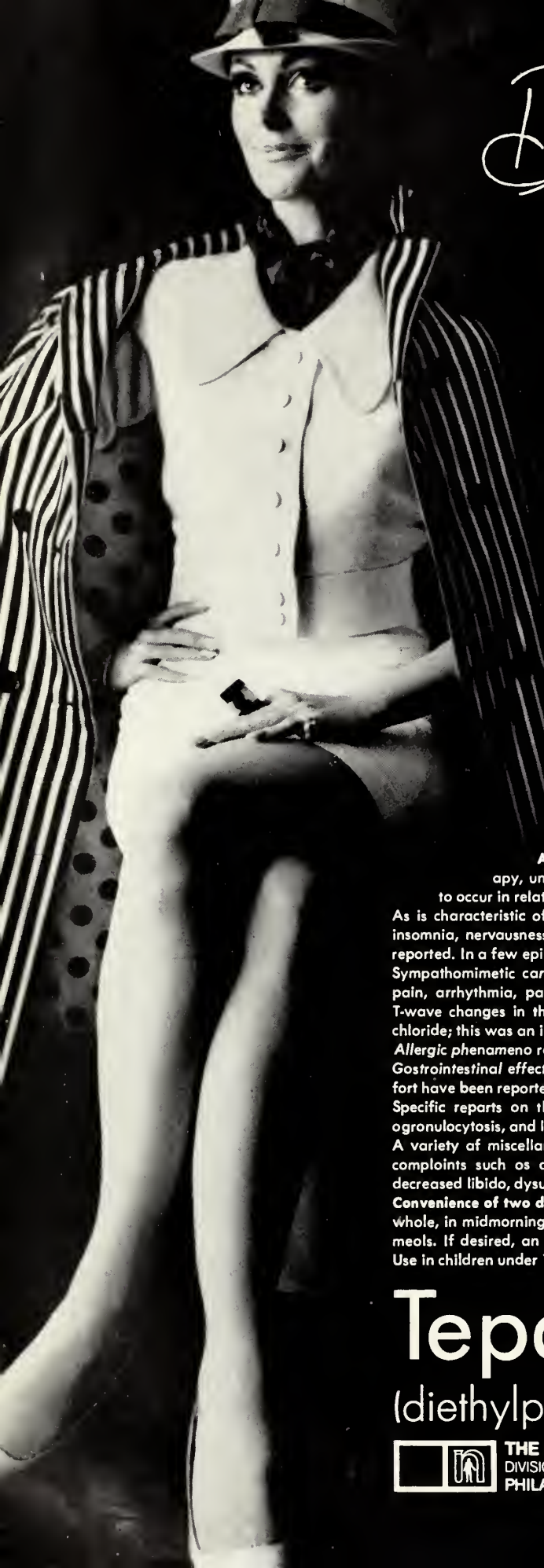
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editorials

Variations In Patients Cooperation With A Medical Regimen

The patients response to a therapeutic regimen obviously depends upon how well he understands the physician's instructions and how accurately he follows them. The physician bases critical decisions in management and even diagnosis on the patients response. He may decide to change the treatment or he may even question the original diagnosis if the patient is not improving. One reason for a program to be ineffective is that the patient is not following it. Thus in order to make a correct decision the physician must be able to assess the degree to which the patient is actually following the regimen outlined.

To evaluate the accuracy of such judgments physicians estimate of a hospitalized patients cooperation with an antacid regimen for peptic ulcer was compared by Caron and Roth¹ with objective measurements of the cooperation of these same patients. These authors had already found previously that patients with peptic ulcer varied widely in their degree of cooperation with an antacid regimen and that the average patient consumed only 40-45 per cent of the medicine prescribed.

In this study, 27 residents estimated their individual patients adherence to an antacid regimen. The physicians estimate were then compared with counts of the bottles of antacid actually consumed by the patients. The median patient took 46 per cent of the prescribed medicine whereas the physicians error of estimate was 32 per cent. Of the 27

physicians, 22 overestimated their patients antacid consumption. Furthermore, the physicians were unable to distinguish those patients who adhered well from those who adhered poorly even when the judgments were restricted only to those in which the physician indicated most confidence. Thus the correlation between estimated and measured antacid consumption clustered about zero! The accuracy did not vary with the amount of medicine prescribed, the number of patients judged, the height of the estimated or measured antacid consumption or the range or variability of the estimate.

It became clear that the ward physicians were unable to estimate the antacid intake of their patients and 22 of 27 over-estimated the levels of the patients cooperation. Furthermore, the physicians ability to distinguish those patients who adhered well from those who adhered poorly was no better than might be expected by chance. When one considers that many patients are on special diets and take several medications, as many as three or four times a day in other diseases besides peptic ulcer Caron and Roth's findings have important implications in all kinds of medical management. Before concluding that a serious gap exists in communication between physician and patient we should review some of the limitations of this study.

It was conducted with hospitalized patients and some medical residents may have assumed that the medicine prescribed in a hospital is almost always taken as ordered. Accordingly despite direct daily contacts, physicians may have failed to make searching observations of patients cooperation that they

THE COVER

The Connecticut Society of American Board Surgeons was founded in 1948 by a group of surgeons for the purpose of promoting cooperation, education and fellowship and to exercise a guiding influence on the development of surgery for the benefit of the people of Connecticut. Membership is open to any surgeon living in Connecticut who is certified by the American Board of Surgery.

The annual meeting in December of each year is devoted to the presentation of scientific papers by members of the society. Some of the papers presented at the meeting of December 4, 1968 appear in this issue of *Connecticut Medicine*.

might have made with out-patients. However, as we all know assessment of outpatients adherence to a dietary and medical regimen may prove more difficult than assessment of the medications taken by hospitalized patients, since a greater variety of unpredictable circumstances may influence the strictness with which out-patients take their medications.

The relative inexperience of ward physicians may have further reduced the accuracy of judgment. However, Caron quotes a current study at his hospital in which three senior physicians were asked to make simple assessment of outpatient antacid intake. The correlation between estimated and measured medicine intake was also low. In another recent study² it was found that medical school instructors anticipated unreasonably high levels of antacid intake and that senior medical students anticipated lower and perhaps more realistic levels of cooperation. Such data do not suggest that assessment of patients cooperation in treatment improves greatly with clinical experience. Perhaps there is little opportunity to improve since data that would permit the correction of errors are readily available to the physician.

A variety of additional factors may have contributed to physicians misjudgment of antacid intake. For example certain patients may have misunderstood the instructors and believed mistakenly that they were cooperating. If they conveyed this direct positive impression to the physician, he might accordingly have misjudged antacid intake. Special difficulties in assessment may also be traceable to the discrepancy in socioeconomic background as between the physician and the patient.

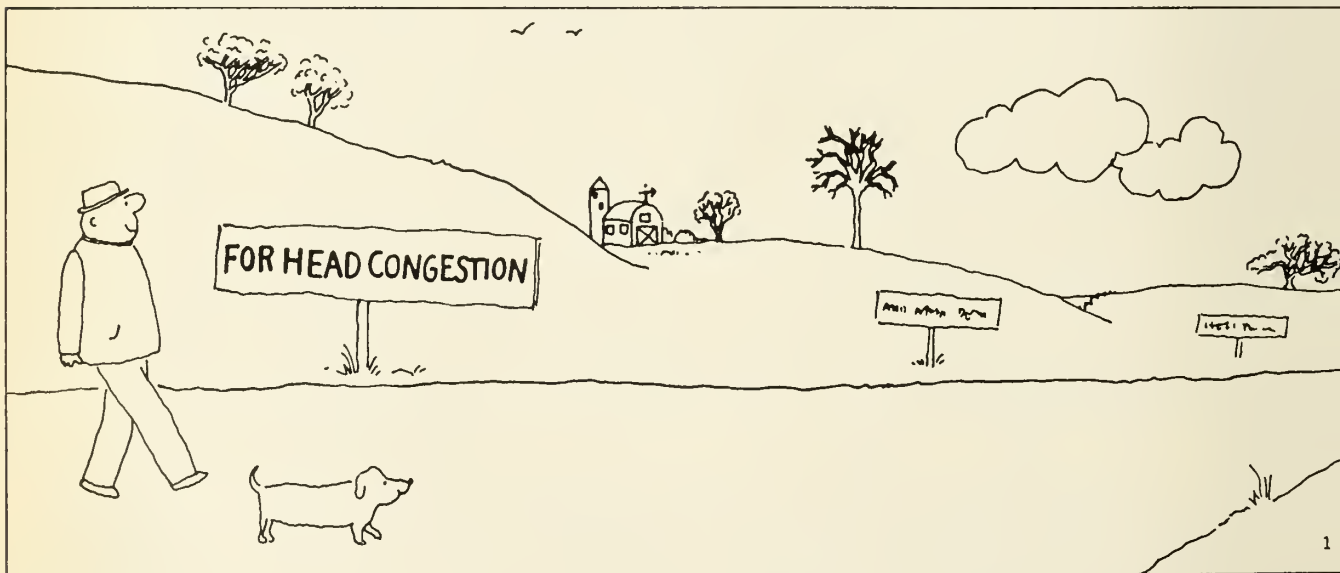
Another possible explanation of the physician's inability to judge antacid intake is that they were not adequately motivated or did not invest sufficient energy in the task. But if this were the explanation, they should not have been able to reproduce their judgments and one might thus have concluded that the physician had no definite conception of their patients antacid intake rather than having inaccurate conceptions. At least some physicians did appear to form impressions that were definite although inaccurate since the reproducibility of their judgments was quite high.

It may be admitted that questions can be raised about the validity and generality of these findings. Nevertheless they do suggest that error can be both common and large. Accordingly studies based on physicians estimation of patients following doctors instructions need to be evaluated critically³ and the practicing physician should be very cautious about judgments that depend even in part on his assessment of patients accuracy on carrying out therapeutic instructions. The physician clearly must take more time in communicating his instructions accurately to the patient. The patients motivation in following them is an unpredictable quality but there must be found some way for the physician to assess accurately how well the patient is carrying out his part of the transaction.

L.H.N.

References

1. Caron, H. S. and Roth, H. P.: Patients cooperation with a medical regimen. JAMA, 203: 922, March 11, 1968.
2. Davis, M. S.: Variations in patients compliance with doctors orders: analysis of conforming between survey re-



sponses and results of empirical investigations. *J. Med. Educ.*, 41: 1037, November 1966.

3. Donabedian, A. and Rosenfeld, L. S.: Follow-up study of chronically ill patients discharged from hospital. *J. Chron. Dis.*, 17: 847, September 1966.

Nutrition, Growth, Infection And Environment

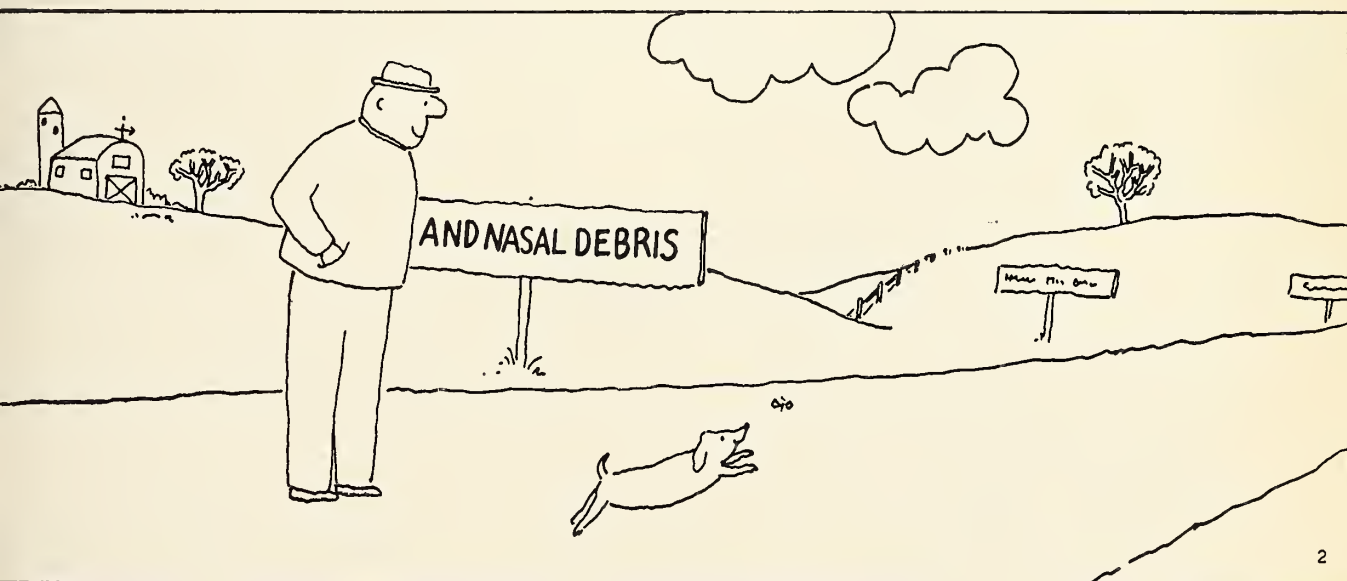
Several pioneering studies on a variety of population groups in whom malnutrition is indigenous have suggested a relation between short stature and low intellectual achievement. This basic condition, malnutrition, occurs primarily among underprivileged populations and thus is located in a particular physical, social and biological environment. This environment and probably malnutrition as well results in an increased frequency and chronicity of infections especially diarrhea among the very young the so-called "weanling diarrhea." Repeated respiratory and gastrointestinal infections produce a cycle in which infection increases metabolic demands, decreases food intake and inhibits absorption of nutrients resulting in a further deterioration of the nutritional state.

The relation between famine and pestilence was recognized in ancient civilizations. Conditions associated with acute famine also provide an environment in which infectious diseases can flourish. Thus the synergism between infectious diseases and malnutrition in humans is both direct and indirect. Infections such as measles may result in severe diarrhea and a high incidence of pneumonia in malnourished children. The reasons for greater severity

of disease and increased incidence of complications could be reduction in immunologic responses when protein deficiency exists. We know that some of the normal components of protective serum, such as complement are reduced.

The major defect to account for the great susceptibility in infection in the malnourished child must be looked for at the cellular level. It is possible that the integrity of the respiratory and gastrointestinal epithelium is so altered as to permit more ready invasion of the body. Then normal inflammatory and healing responses are more or less inhibited also. In kwashiorkor reduced inflammatory response has been clearly demonstrated. The child enters the hospital without showing signs and symptoms of infection. Once rehydrated and nutritional requirements replenished only then do the physical signs of infection become obvious and the signs of inflammation appear. The similarity between the malnourished child and the immature infant is striking. In the immature infant little inflammation around the site of an infection may occur. The delayed hypersensitivity response is suppressed and there appears little tendency for the invading organism to be localized. All these factors result in increased frequency of infection, increased severity of disease and disease produced by organisms which under normal circumstances might not be considered pathogenic.

Furthermore, certain infections in malnourished children may produce severe and prolonged hypoglycemia which in itself can cause brain damage. In addition infection tends to accentuate various biochemical deficits of children with malnutrition.



This in turn presumably renders the patient more susceptible to further infection. Finally is the fact that many infectious diseases or even the therapy used in treatment may result in damage to the central nervous system without this effect necessarily being evident during the acute illness.

Infection and malnutrition thus act synergistically to produce a chronically and recurrently sick child less likely to react to sensory stimuli from his already inadequate social environment. In this way a third factor sensory and emotional deprivation related to illness and environment becomes significant. Studies among different cultures have demonstrated that one of the more important factors contributing to the intellectual development of the child is the level of maternal education. This influence becomes progressively stronger as the child grows older. Furthermore, studies of females of severely malnourished children has indicated that the majority of these mothers themselves have low intelligence quotients.

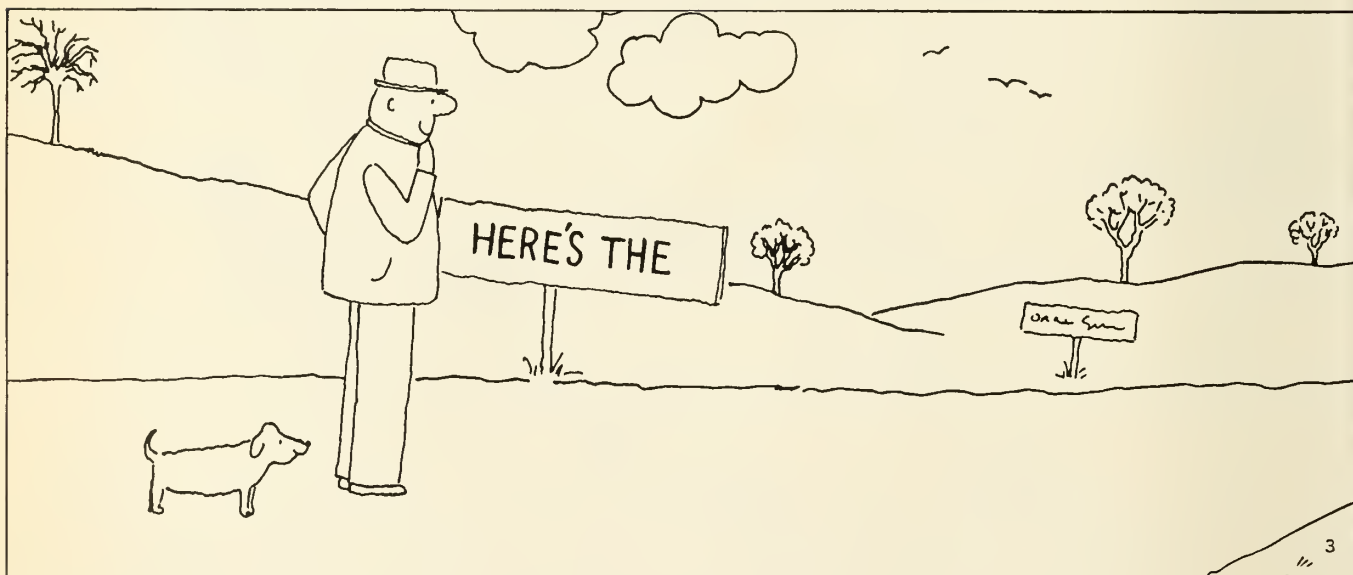
Socioeconomic factors also intervene indirectly. Children suffering from severe malnutrition generally come from homes where the immediate economic pressures are such that the parents cannot provide the child with the stimulation necessary for optimal intellectual development. Thus far studies of human populations generally have not permitted the investigator to separate the effects of malnutrition from infection and from environmental factors such as lack of intellectual stimulation and other socioeconomic conditions.

In animals pathologic changes quite similar to those accompanying malnutrition can be produced

by placing the animal in an environment entirely free of stimulation and by preventing him from exploring it. There are infections associated with hypoglycemia or severe electrolyte disturbances as well as recurrent infections (particularly those affecting the nervous system, lungs or gastrointestinal tract) which may act to retard physical growth and may produce lesions similar to these observed in simple malnutrition.

It is obvious why it is exceedingly difficult to design field studies which would unequivocally decide whether human malnutrition results in permanent impairment of learning and adaptive behavior. Of course from a purely pragmatic standpoint this probably makes little difference. If adequate nutrition in early childhood diminishes the incidence of infection as well as the opportunity for sensory and cultural deprivation, the end result might be much the same. To compound the difficulty, observations would have to be carried on for several decades in order to provide a complete answer. In animals we already know that poor nutrition of the infant female can affect the development of her offspring born many years later.

What we need to know is the crucial time in development when malnutrition causes its major effects as well as the qualitative and quantitative factors involved. We need more studies on psychological testing. We need to know about how much undernourished infants recover once their nutrition is restored. What is their behavior during rehabilitation and how much recovery can we expect. We know something about the biochemical development of the nervous tissue. But little is



known of the effects of nutrition about the physiological processes of these organs and we need more adequate information as the relation between mentation and cellular metabolism.

If backwardness of some societies is related to the inhibitory effects of malnutrition on physical, mental and emotional development one would still have to determine how this defect can be corrected. The answer is more complicated than by simply furnishing food. Some cultures believe that foods we consider important to young children are harmful to theirs. So they will sell or trade nutritional supplements for substances thought to be more useful or of greater importance to the adult. Where tradition rather than education determines food utilization we must understand the forces behind the tradition before positive approaches can be undertaken. In some cultures the dominant group might look with favor upon undernutrition as the best way to keep their people apathetic and unrebellingous.

L.H.N.

References

1. Platt, B. S., Heard, C. R. C. and Stewart, R. J. C. in Mammalian protein metabolism. H. N. Munro, J. B. Ellison Eds. Academic Press, New York. 1964. Vol. 2.
2. Gordon, J. E. in Prevention of mental retardation through control of infectious disease. U.S. Public Health Serv. Publ. No. 1962 (1968).
3. Eichenwald, H. F. in Malnutrition learning and behavior. N.S. Scrimshaw and J. E. Gordon Eds. (MIT Press Cambridge, Mass.) 1968.
4. Nahum, L. H.: Nutrition of the fetus and the intelligence of the child. *Conn. Med.*, 33: 76, February 1969.
5. Eichenwald, H. F. and Fry, P. C.: Nutrition and learning. *Science*, 163: 644, February 14, 1969.

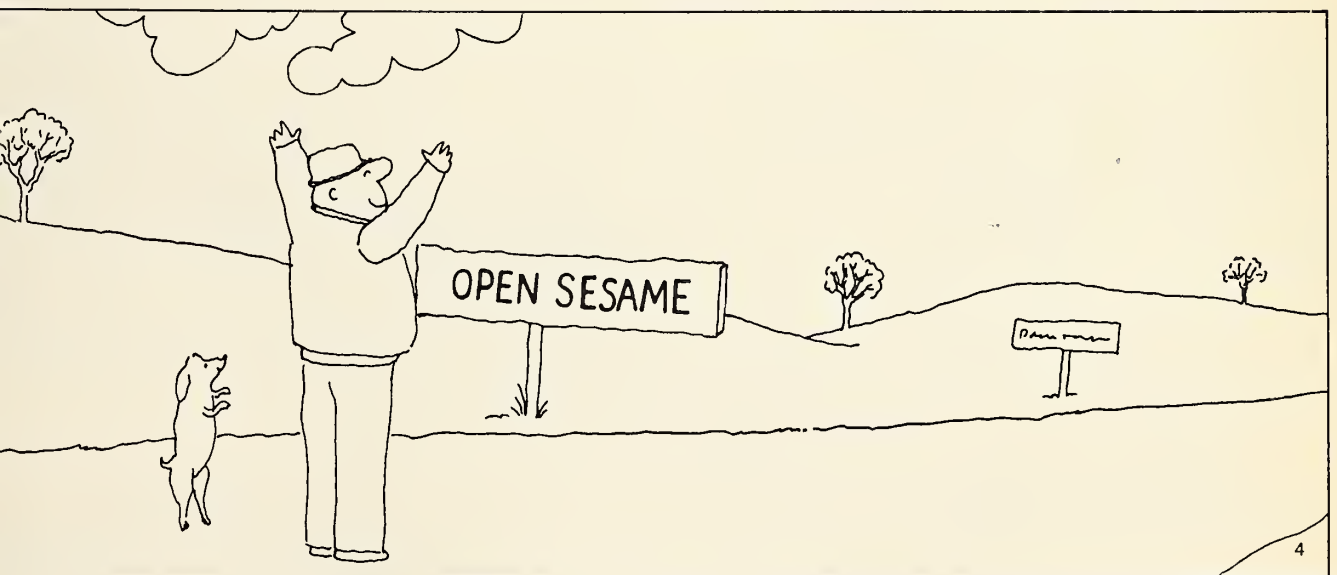
Platelets In Thrombosis

The status of this problem was recently summarized as follows: "arterial thrombosis is a common event with sinister consequences and despite its frequency we do not understand the thrombotic process nor do we have any prophylactic or therapeutic measures as our command."

The so-called red thrombus is an occlusive mass composed of all blood cellular elements distributed in a random fashion held tightly together with fibrin and contains within it a significant amount of plasminogen. It typically forms in patients with hypercoagulability and when the velocity of flow through a vein is considerably reduced. Embolization of fragments of red thrombi to other sites in the vascular tree is an important complication. There are many similarities between red thrombi and the clot that forms normally in a test tube.

The blood vessel wall probably does not contribute to red thrombus formation and the underlying pathogenesis may be a local activation of the intrinsic prothrombin activator system, that is either local or general hypercoagulability. The mechanism by which the intrinsic system is activated remains to be elucidated. The most important factor appears to be stasis. Thus the red thrombus forms mainly in the venous channels or distal to an occlusive arterial lesion where the flow of blood has almost ceased.

The lesion of occlusive arterial disease is the white thrombus which consists mainly of platelets and a few fibrin strands. Thus platelets have the important role in the formation of the white



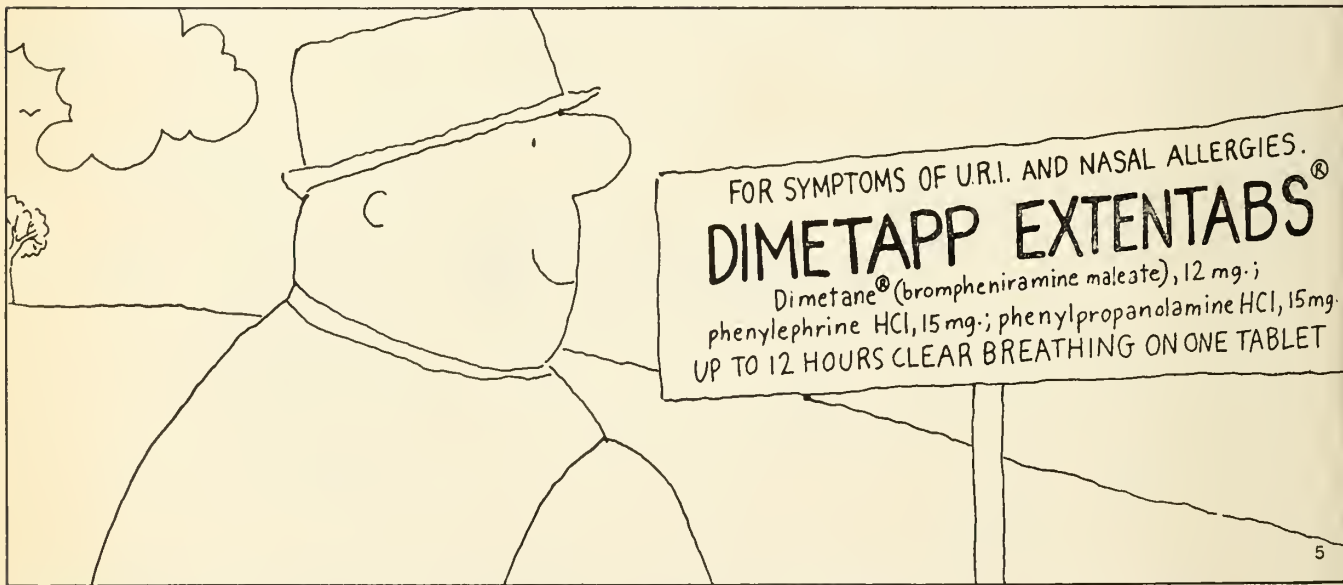
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thrombus. Morphologically the white thrombus resembles closely the normal hemostatic plug that terminates hemorrhage. Thus one can think of occlusive arterial disease as an undesirable form of hemostasis. The initial event is an interaction between the platelet membrane and an abnormal blood vessel wall where the endothelial layer has presumably been disrupted exposing the underlying connective tissue collagen. As in the hemostatic process blood coagulation is not involved in these early reactions. Thus in persons with coagulation disorders, these do not interfere with development of arterial occlusive disease. Furthermore, anticoagulants which work effectively to prevent the red thrombus have proved to be relatively ineffectual in the treatment of arterial thrombosis.

Mural thrombi have been produced experimentally in the carotid arteries of swine and studied in great detail. After one hour the thrombus was composed of a densely packed platelet mass surrounded by fibrin strands. In the course of 24 hours the platelets separated from each other and underwent dissolution and increasing amounts of fibrin were seen between them. At the same time polys and mononuclear cells were seen on the luminal surface and within the thrombus itself. Areas of endothelism beneath the thrombus showed degenerative changes and began to disappear. In 2-4 days the fibrin was reduced and cellular debris removed by phagocytosis. Finally new endothelium appeared on the luminal surface. In 6-8 days and ending in two weeks there was internal thickening that consisted of accumulated smooth muscle cells, collagen, and elastic fibers covered over with endothelium.

Thus a thrombus examined hours or days after its formation does not resemble the initial platelet mass and experimental thrombi induced by i.v. administration of ADP do not resemble those induced by damage to the blood vessel wall. ADP clearly has a control role in the aggregation phenomenon, but additional factors are necessary in the production of arterial thrombosis. It would be important to ascertain whether and under what conditions platelet masses that form in the arterial circulation may be swept away spontaneously, since there is some experimental evidence that this disintegration does indeed occur.² Could it be quantitatively related to ADP liberation? This appealing concept has in fact stimulated a search for drugs that interfere with the action of ADP on platelets.³ However, exposed collagen also increases platelet aggregation, so that the problem is more complex since several factors interact in the formation of the platelet thrombus. It would of course also be profitable to understand the mechanism whereby platelets in a thrombus begin to disintegrate so we could finally accelerate the dissolution of a thrombus already formed.

There are laboratory methods for studying platelet physiology in hemostrasis which should help us to evaluate platelet behavior in arterial thrombosis. One is to analyze platelet adhesion to a blood vessel wall. Most studies of platelet behavior however necessarily involve not in-vivo but in-vitro procedures. Passage of whole blood through columns of glass beads. But when a change is found in platelet adhesiveness by this method it is relatively non specific and the information it offers about throm-



botic disease is limited. Then there are tests of platelet aggregation in platelet rich plasma in response to physiological and pharmacological agents. In such procedures, however, one cannot know whether the platelets under study truly represent those in the circulation.

Platelet electrophoretic mobility does offer important advantages over other techniques in discovering abnormal patterns which have already been uncovered in acute illnesses, certain chronic disorders and occlusive vascular disease. The field of arterial occlusion is still wide open, the stakes are high but as was said in the opening sentence we do not have any prophylactic or therapeutic measures at our command.

L.H.N.

References

1. Jørgensen, L., Rowell, H. C., Horig, T. and Mustard, J. F.: Resolution and organization of platelet-rich mural thrombi in carotid arteries of swine. *Am. J. Path.*, 51: 681, 1967.
2. Hampton, J. R.: Study of platelet behavior and its relevance to thrombosis. *J. Atheroscler. Research*, 7: 729, 1967.
3. Marcus, A. J.: Platelet function (third of three parts). *New Eng. J. Med.*, 280: 1330, June 12, 1969.

Alternate Day Prednisone Therapy

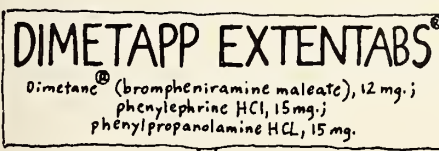
Attempts have been made to minimize the well known and potentially serious side effects of corticosteroids ever since they have been found to be effective therapeutic agents in the treatment of many human inflammatory diseases. Increased susceptibility to infection, pituitary-adrenal suppression, diabetes mellitus and osteoporosis have caused

investigators to search for methods to avoid such side effects of glucocorticoids. Primarily the methods employed depended upon reducing the corticosteroid dose to near physiological levels. But the result often was poor control of the underlying disease.

Over the past few years attempts have been made to reduce steroid side effects by varying the method of corticosteroid administration. One such schedule was to have the patient take the dose for four days and stop three days. However, too many troublesome side effects eventually developed in many patients. There is now gaining increasing clinical acceptance the method of using corticosteroids on alternate days. By this means the disease has been satisfactorily controlled and most side effects have been minimized.

McGregor¹ has recently reported not merely the reduction in the endocrine and metabolic side effects of alternate day steroid administration but also the effect of intermittent steroid administration on delayed hypersensitivity responses as well in 12 patients who received alternate day prednisone therapy. The importance of these latter observations was the effort to determine whether patients retain their resistance to other infections or lose them as they do on continuous corticosteroid therapy.

McGregor's observations show that alternate day administration of prednisone does not inhibit delayed-type skin reactivity and that sensitization to a new antigen could be produced although to a degree somewhat less than usually seen in normal volunteers. The patients who were switched from daily to the alternate day regimen not only main-



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PRECAUTIONS: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension.

SIDE EFFECTS: Hypersensitivity reactions including skin rashes, urticaria, hypotension and thrombocytopenia, have been reported on rare occasions. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered.

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tained their reactivity but also exhibited some increase in skin reactivity. The question, of course, arises whether preservation of delayed hypersensitivity responses will be associated with a decrease in morbidity from infection. It probably will, but the final answer to this question requires a much larger follow-up period. Thus far the authors have not seen any increase in the number of infections in any of the patients on alternate day steroid schedule over the entire course of their studies.

There has been debate over the years about the role of delayed hypersensitivity in the histologic development of the granulomatous inflammatory response. In this study several patients did have granulomatous inflammation, one sarcoidosis and several with hepatic granulomas of unknown etiology, who exhibited proved regression and disappearance of such lesions on the alternate day prednisone regimen.

Other corticosteroid effects were markedly reduced. The adrenal responsiveness to stimulation with ACTH was normal. Plasma ACTH concentrations were also normal meaning that the pituitary was not suppressed. Patients who had normal glucose tolerance did not develop any abnormality in the course of the study. Those patients with pre-existing diabetes showed improvement in manageability on alternate day steroid administration.

There is one note of caution that should be made about ophthalmologic complications, because two of the twelve patients did develop posterior subcapsular opacities on alternate day prednisone. Obviously careful ophthalmologic follow-up studies are indicated in all patients on steroids for prolonged periods whether they are on a daily or alternate day schedule.

Most rewarding has been the sustained control of the underlying inflammatory disease attained largely without glucocorticoid side effects. The authors gave double the daily amount when starting the alternate day schedule. The change from daily to alternate-day prednisone can take as much as several months to accomplish because of exacerbation of disease on the off day as the alternate day dosage was diminished. In such cases addition of aspirin, very gradual reduction of the dose and acceptance of some fever and myalgia on the off days for several cycles become necessary.

In the light of these studies, a trial of alternate day therapy should be given to any patient requiring prolonged prednisone administration. Furthermore, a patient who requires daily therapy at the outset to control symptoms, could very well have

regular attempts to switch to an alternate day regimen.

L.H.N.

1. McGregor, R. R., Sheagren, J. N., Lipsitt, M. B. and Wolff, S. M.: Evaluation of alternate day prednisone therapy *New Eng. J. Med.*, 280: 1427, June 26, 1969.

Increasing Muscular Strength In Athletes

Androgens exert a positive effect on muscle growth in various animal species, for example hypertrophy of certain muscles in immature guinea pigs who have received testosterone propionate. Likewise, increased weight gains in steers resulted when they were given weekly 1 M. injections of 1 mg. of testosterone propionate per kg. of body weight weekly.¹ Such experiences have led to the use of anabolic steroids by athletes in the hope of developing increasing strength. This practice has become increasingly widespread especially by those in activities where strength is the prime factor for successful performance. In fact many instances of extraordinary and rapid improvement have been reported but the evidence is entirely empirical.

Little is known about possible long term side effects in adults. When individuals are physically immature they can expect possible acceleration of epiphyseal ossification and manifestations resembling macrogenitosomia praecox. These two results of androgen administration are severe contraindications to its use in teenagers.

Anabolic agents have been used for some time for patients recovering from illness or after surgery, for treatment of osteoporosis, fracture healing, severe burns and muscular dystrophy in the hope of building protein tissue and for increasing muscle mass.² Anabolic agents have also been credited with having an important effect in stimulating the appetite and imparting a feeling of well-being. Even though there is little data on the use of anabolic steroids by athletes, there is sufficient clinical evidence that the anabolic potencies of such drugs should on theoretical grounds stimulate muscle hypertrophy and increase strength in normal healthy men.

Johnson and O'Shea² found it difficult to obtain volunteers who were willing to take the steroid, particularly because of the paucity of knowledge concerning side-effects. There was a widespread fear that steroid treatment might reduce the sexual drive. However, the researchers did find 12 men who volunteered to take the steroids and 12 unwilling but who consented to act as controls. In the first three weeks all the subjects became accustomed

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Contraindicated: In individuals hypersensitive to any of the components of this drug.

Warnings: If renal impairment exists, even usual doses may lead to excessive systemic accumulation and possible liver toxicity. In such patients, lower than usual doses are indicated and for prolonged therapy oxytetracycline serum level determinations may be advisable.

Terramycin may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.

Use of oxytetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of teeth. This effect occurs mostly during long-term use of the drug, but it has also been observed in usual short-treatment courses.

During treatment with tetracyclines, individuals susceptible to photodynamic reactions should avoid direct sunlight. Discontinue therapy at first evidence of skin discomfort.

Note: With oxytetracycline, phototoxicity is not believed to occur and photoallergy is very rare.

Precautions: Use of broad-spectrum antibiotics occasionally may result in overgrowth of nonsusceptible organisms. Where such infections occur, discontinue oxytetracycline and institute specific therapy.

As with all intramuscular preparations, Terramycin Intramuscular Solution should be injected well within the body of a relatively large muscle. **Adults:** The preferred sites are the upper outer quadrant of the buttock (i.e., gluteus maximus), or the mid-lateral thigh. **Children:** It is recommended that intramuscular injections be given preferably in the mid-lateral muscles of the thigh. In infants and small children the periphery of the upper outer quadrant of the gluteal region should be used only when necessary, such as in burn patients, in order to minimize the possibility of damage to the sciatic nerve.

The deltoid area should be used only if well developed such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-thirds of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.

Increased intracranial pressure with bulging fontanelles has been observed occasionally in infants receiving therapeutic doses of the drug, but such signs and symptoms have disappeared rapidly on cessation of treatment with no sequelae.

Adverse Reactions: Subcutaneous and fat-layer injection may produce mild pain and induration which may be relieved by an ice pack. Very mild gastrointestinal disturbances, not requiring discontinuance of the drug, may occur occasionally. Allergic reactions, including anaphylaxis, rarely have been observed.

Dosage: **Adult:** The optimal dosage varies, depending on the type and severity of infection. Unless otherwise specified, a dose of 100 mg. every 8 to 12 hours, or a single daily dose of 250 mg. should be adequate for the treatment of most mild or moderately severe infections. In severe infections, 100 mg. every 6 to 8 hours, or 250 mg. every 12 hours may be necessary.

Serum levels obtained by the recommended dosages are comparable to those provided by the oral dosage of 1 to 2 Gm. daily in adults. Antibiotic therapy should be continued for at least 24 to 48 hours after all symptoms and fever have subsided.

In certain diseases specific courses of therapy may be recommended as a general guide. In primary and secondary syphilis for example, the daily administration of 2 Gm. oxytetracycline, orally, in divided doses for two weeks has given good results. In cases of gonococcal infection two intramuscular injections of 250 mg. each, or one intramuscular injection of 250 mg. combined with one gram given orally as a single dose, will usually suffice, but repetition of this therapy will be required in an occasional case.

In the treatment of hemolytic streptococcal infections, therapy should continue for at least 10 days to prevent development of rheumatic fever or glomerulonephritis. In the treatment of staphylococcal infections indicated surgical procedures should be carried out in all cases.

Pediatric: A dosage of 3 mg./lb./day in two doses has been found satisfactory in the treatment of most mild to moderately severe infections. For more severe infections, higher dosages may be indicated and should be adjusted accordingly.

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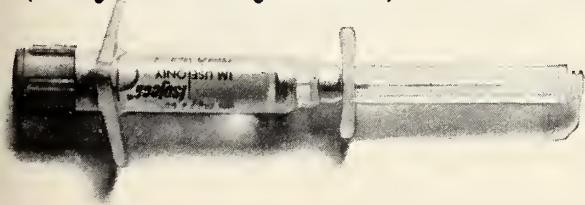
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Fire victim. Examination reveals second degree burn of lower leg. To combat shock, restore circulatory volume and replace protein loss, plasma is administered. Local pressure dressing applied. Limb elevated to limit the flow of lymph. About 36 hours after admission the patient develops an elevated temperature and complains of pain at the site of the lesion. Dressing removed. A suppurating slough area has developed over part of the burn. A swab specimen is taken for culture and the slough area is debrided. Antibacterial treatment is begun with Terramycin I.M. Days later, recovery is progressing, and the laboratory report shows a mixed infection with a predominance of susceptible coliform bacteria, confirming the therapeutic choice. Terramycin therapy is continued until all signs of infection disappear.

Experience has shown that Terramycin offers special advantages in treating bacterial infections complicating burns, when strains of causative organisms are susceptible. Broad-spectrum antibacterial coverage. Activity unaffected by penicillinase. Rapidly achieved therapeutic blood levels. Proven tissue toleration.

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to a training regimen and an adequate degree of strength fitness was developed. In the last three weeks one group was given 5.0 mg. of methandrostenolone (dianabol)³ twice daily.

The training program of the treatment and control subjects were identical. The effectiveness of the three week steroid treatment on the development of strength and muscle hypertrophy was determined by seven measurements including static and dynamic strength, O₂ uptake, blood lipids, blood chemistry profile, and skin thickness. Dynamic and static strength increased significantly in the treated individuals and the authors concluded that the treatment with anabolic steroids is apparently an effective way for developing muscular strength. Their investigation gives an experimental basis for other reports from athletes who on an empirical basis seemed to develop muscular hypertrophy resulting from the use of anabolic steroids.

The control group with the same degree of exercise gained but .29 kg. whereas the treated group gained 2.48 kg. or almost ten times as much. This weight gain was not due to increase in fat and therefore must have been due to increase in lean body mass. There was also significant increase in oxygen uptake ability in the treated individuals and this suggests that the steroids could improve performance in events requiring endurance. They found also a decrease in free cholesterol in the treated group. They conclude that a combination of high protein intake, steroid treatment, and heavy muscular exercise accelerated protein synthesis in the muscular tissue.

No side effects were noted. There was some increase in urine production. Some subjects felt an extra degree of tension but one must remember that they were engaged in a strenuous training program. One unexpected finding was a near absence of normal muscle soreness and stiffness in the treated group following the training sessions. It thus appears possible to train at near maximum five or six times a week during the treatment without undue fatigue. Furthermore, the fears of reduction in sex drive were entirely unfounded.

The authors advise that such treatment be used cautiously, however, until more information is available on the physical effects in a larger sample of humans than the twelve in their series. Some of the future work should attempt also to analyze possible psychological consequences of the treatment especially because the brain is such an active synthesizer of protein.

L.H.N.

References

1. Burris, M. J., Bogart, R. and Oliver, H. W.: Quoted by Johnson et al.
2. Johnson, L. C. and O'Shea, J. P.: Anabolic steroid: effects on strength development. *Science*, 164: 957, May 23, 1969.
3. New Drugs. American Medical Assoc., Chicago, Ed. 3, pp. 401-404, 1967.

Acne Vulgaris

A disease does not have to be fatal, incurable or physically crippling to be devastating. Acne vulgaris causes emotionally devastating effects by disfiguring the face that the adolescent turns to the world he is just beginning to confront.—Freinkel.

Clinically there are two types of acne lesions which occur in relation to the pilosebaceous follicles. One is the comedo which is a dilated follicle filled with cellular debris and micro-organisms and becomes a blackhead if the orifice is patulous. The second lesion is inflammatory, begins with a small papule, evolving into a pustule, and when deeper in the dermis, into a pseudocyst.

Inflammation develops in each type and goes through two phases. At first there is a focal inflammation of the wall of the follicle and lymphocyte infiltrate into the subjacent dermis. The inflammation may progress, destroy the wall of the follicle and produce massive leakage of the follicular content into the dermis. An inflammatory reaction is now provoked by the contents of the follicle further damaging the wall, with further leakage and more severe and more destructive inflammation and repair.

The question arises as to which of the three contents of the follicle it is that provokes the inflammatory reaction, is it the bacteria, the desquamated epithelium or the sebum itself. The bacteria, of course, could provoke a secondary infection. The desquamated epithelium, which seems inert, do contribute to the inflammatory response once the cells enter the dermis. However, it is the sebum itself which Freinkel¹ points out that has the primary role in the initiation of the inflammation. This can be shown by injecting sebum lipids and obtaining an inflammatory response. The fraction of sebum most irritating is free fatty acids (FFA) and it is probably this component which initiates inflammation and disruption of the follicle.

Free fatty acids result from hydrolysis of triglycerides and the source of the lipolytic activity seems to be the resident flora, for if one can suppress the bacteria by tetracycline the result is reduction of

the concentration of FFA without affecting sebum production. Both the normal cutaneous staphylococcus albus and Corynebacterium acnes have been shown to elaborate lipases.

On the basis of these data Freinkel has formulated a hypothesis regarding the pathogenesis of acne vulgaris. At puberty under the influence of androgens the sebaceous glands develop and the characteristic sebaceous follicle is formed. As a part of this response follicular walls hypertrophy and some of the enlarged walls mechanically block the flow of sebum from the follicle. Bacteria flourish in this nutrient-rich environment and C. acnes is especially favored by the relative anerobiasis of the follicle. The bacteria elaborate lipolytic enzymes which act on sebum triglycerides to produce FFA. This in turn acts as the initiator of the inflammatory response.

The variables affecting manifest acne would consist of the absolute amount of sebum triglycerides, and their fatty acid composition, the nature of the flora and its intrinsic lipolytic activity, the effect of temp, pH, and other factors in the milieu on lipase activity, the vulnerability of the follicular wall to chemical insult and the response of the host

to inflammatory provocation.

Thus far few of the clinical attributes of acne have been analyzed in terms of these variables. As yet there is no immediate explanation for the predisposition of some persons to acne, its cyclic course in females, the apparent adverse reactions to certain foods such as carbohydrates, the beneficial effects of ultraviolet light and the spontaneous remission after adolescence.

If we accept that it is the interaction between sebum and micro-organism in the pathogenesis of acne, then the rational approaches to therapy suggest themselves. We might direct our efforts towards either suppressing the production of sebum or interfering with the lipolytic activity of bacteria in the skin. Of the many therapeutic modalities now in use to control the disease, lotions and topical agents, we do not really know how they work on the acnegenic process because these agents do not appear to affect the sebum production. Those that do succeed in suppressing sebaceous gland activity like X-rays and estrogens are understandingly successful in suppressing acne.

On theoretical grounds broad spectrum antibiotics such as tetracyclines should be effective and

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WARNINGS: Patients should be warned against driving a car or operating machinery or apparatus requiring alert attention, and that response to alcohol may be potentiated.

PRECAUTIONS: Suicide is always a possibility in mental depression and may remain until significant remission occurs. Supervise patients closely in case they may require hospitalization or concomitant electroshock therapy. Untoward reactions have been reported after the combined use of antidepressant agents having various modes of activity. Accordingly, consider possibility of potentiation in combined use of antidepressants. Not recommended for use in children. Mania or hypomania may be precipitated in manic-depressives (perphenazine in TRIAVIL seems to reduce likelihood of this effect). If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Caution patients about errors of judgment due to change in mood.

SIDE EFFECTS: Similar to those reported with either constituent alone. **Perphenazine:** Should not be used indiscriminately. Use caution in patients with history of convulsive disorders or severe reactions to other phenothiazines. Likelihood of untoward actions greater with high doses. Closely supervise with any dosage. Side effects may be any of those reported with phenothiazine drugs: blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); extrapyramidal symptoms (opisthotonos, oculogyric crisis, hyperreflexia, dystonia, akathisia, dyskinesia, parkinsonism) usually controlled by the concomitant use of effective antiparkinsonian drugs and/

or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine; severe, acute hypotension (of particular concern in patients with mitral insufficiency or pheochromocytoma); skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angio-neurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; endocrine disturbances (lactation, galactorrhoea, disturbances of menstrual cycle); grand mal convulsions; cerebral edema; altered cerebrospinal fluid proteins; polyphagia; paradoxical excitement; photophobia; skin pigmentation; failure of ejaculation; EKG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonie-like states; autonomic reactions such as dryness of the mouth, headache, nausea, vomiting, constipation, obstipation, urinary frequency, blurred vision, nasal congestion, and a change in the pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude; muscle weakness; mild insomnia; significant unexplained rise in body temperature may suggest intolerance to perphenazine, in which case discontinue. Antiemetic effect may obscure signs of toxicity due to overdosage of other drugs or make diagnosis of other disorders such as brain tumors or intestinal obstruction difficult. May potentiate central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol), atropine, heat, and phosphorous insecticides. **Amitriptyline:** Careful observation of all patients recommended. Side effects include drowsiness (may occur within the first few days of therapy); dizziness; nausea; excitement; hypotension; fainting; fine tremor; jitteriness; weakness; headache; heartburn; anorexia; increased perspiration; incoordination; allergic-type reactions manifested by skin rash, swelling of face and tongue, itching, numbness and tingling of limbs, including peripheral neuropathy; activation of latent schizophrenia (however, the perphenazine content may prevent this reaction in some cases); epileptiform seizures in chronic schizophrenics; temporary confusion, disturbed concentration, or transient visual hallucinations on high doses; evidence of anticholinergic activity, such as tachycardia, dryness of mouth, blurring of vision, urinary retention, constipation, paralytic ileus; agranulocytosis; jaundice. The antidepressant activity may be evident within 3 or 4 days or may take as long as 30 days to develop adequately, and lack of response sometimes occurs. Response to medication will vary according to severity as well as type of depression present. Elderly patients and adolescents can often be managed on lower dosage levels.

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often but not always are. This is so because the organisms responsible for FFA production are uniformly sensitive to this antibiotic. When broad spectrum antibiotics are not as successful their therapeutic failure may be due to the difficulty of getting the drug to the bacteria. Orally administered drugs must be excreted through the skin into the follicle to reach the bacteria. Since the cutaneous barrier is impenetrable, the antibiotic must be bound to cells and egress by desquamation or sebum excretion. This is a cumbersome route but fortunately is indeed followed by tetracycline. It is this fact which may explain the rather selective effects of these agents both on acne and the concentration of FFA.

L.H.N.

Reference

1. Freinkel, R. K.: Pathogenesis of acne vulgaris. *New Eng. J. Med.*, 280: 1161, 1969.

Myasthenia Gravis An Auto-Immune Disease Of The Thymus Medulla

Myasthenia gravis a disease characterized by progressive muscle weakness is now thought to be an auto-immune process. Patients with this disease have an increased incidence of other auto-immune diseases also have autoantibodies directed against the H band striations of skeletal muscle which cross react with the myoid cells in the thymic medulla. In short thymic abnormalities are constantly found in myasthenia. There appear to be lymphoid germinal centers in the thymic medulla and increased lymphocytes in the medulla of all cases.

The normal thymus is a lymphoid organ except that the thymic lymphocytes differ from peripheral lymphocytes in that they are less competent immunologically and do not usually produce antibody or react so well with antigen. For this reason thymic lymphocytes usually do not respond in-vitro to phytohemagglutinins (PHA) which however stimulates the proliferation of immunologically competent peripheral lymphocytes.¹

A model of myasthenia can be produced in guinea pigs by immunizing them with thymic tissue. They develop a neuromuscular block similar to that in myasthenia gravis and infiltration of the thymic medulla by increased numbers of lymphocytes. This so called experimental auto-immune thymitis causes a substance termed "thymin" to be released in excess from the inflamed thymus and it is this that is thought to cause the neuromuscular block.²

The thymus of guinea pigs with such an experimental auto-immune thymitis also contain an in-

creased number of lymphocytes which now are also responsive to PHA in-vitro. Oppenheim and Goldstein prepared tissue antigens from thymus muscle, spleen, liver, kidneys of young guinea pigs and injected them into the foot pad. After two weeks the animals were killed and examined. Animals immunized with thymus showed histological changes of thymitis. Immunization with muscle also caused thymitis. It was the author's view that both muscle and the myoid cells of the thymus have an antigen in common. However, the thymus is more effective than is muscle in causing thymitis.

In the case of immunologically produced thyroiditis, peripheral lymphocytes sensitized with antigens present in a gland infiltrate cross react with the antigen in that gland. Similarly lymphocyte aggregation in the thymic medulla probably reflect the appearance of increased numbers of peripherally sensitized lymphocytes in the thymus in the course of an experimentally induced inflammation, since they now react to PHA in-vitro.

Oppenheim and Goldstein's findings extend the analogy between experimental auto-immune thymitis and human myasthenia gravis. In both conditions we find an increased number of lymphocytes in the thymus which are immunologically competent. These findings support the idea that the thymic pathology of both consists of an infiltration of immunologically competent lymphocytes that is the cause of chronic inflammation or thymitis.

If myasthenia gravis is indeed an auto-immune disease then it should respond to steroids as do other auto-immune diseases in the sense that the process may not progress or even regress following such therapy.

L.H.N.

1. Thorbecke, G. J. and Cohen, M. W.: *The thymus* (Ed. by Defendi, V. and Metcalf, D.) 33, Wistar Institute Press, Philadelphia, 1964.
2. Oppenheim, J. J. and Goldstein, G.: Enhanced thymic lymphocyte response to phytohemagglutinin in experimental auto-immune thymitis. *Nature*, 222: 192, April 12, 1969.

Carbon Disulphide And Coronary Heart Disease

Dietary factors in the genesis of atherosclerosis have been enlarged from cholesterol alone which dominated the etiologic arena for two decades to triglycerides and saturated fatty acids and minor dietary competitors such as sucrose and coffee. Prominent among the non-dietary factors are smoking, lack of exercise, nervous tension, and of course such predisposing constitutional factors as hypertension, lipidemia, diabetes and gout. To this list

can be added drugs which enhance clotting mechanisms thus facilitating thrombosis in a narrowed vessel.

A recent study by Tiller et al¹ suggests that not only the life we lead or the food we eat but also the air we breathe may be incriminated. These investigators studied the mortality from cardiovascular disease among workers in the British rayon industry. Between 1933-1962, 42 per cent of deaths among male workers exposed to carbon disulphide (CS₂) in three viscose rayon factories in England and Wales were due to coronary heart disease (CHD). The proportion for other rayon workers of comparable age was 24 per cent. The highest mortality rate in men employed over ten years was found in the spinning department where the workers were constantly exposed to CS₂. This gas then emerges as a probable specific industrial risk in the causation of CHD.

Toxic effects from exposure to CS₂ have been recognized for over a century. Neurological syndromes, psychoses, encephalopathy, and polyneuritis were first reported in the rubber industry in which CS₂ was used as a softening agent. During the past fifteen years there have been several reports from other countries of viscous rayon workers developing atherosclerosis at a relatively early age. Animal experiments on rabbits exposed to CS₂ produced changes in the coronary vessels such as thickening of the endothelium, extra mural hemorrhage with hyalinization and sclerosis of the intima. It is not surprising therefore that Tiller could uncover evidence of an occupational risk of CHD from long term exposure to low concentrations of CS₂.

If CS₂ is indeed responsible for the increased incidence of CHD in viscose rayon workers what is its possible mechanism of action. High blood cholesterol levels with an increase in the B lipoprotein fraction have been observed in this group.² Several other studies have suggested a link between CS₂ exposure, lipid metabolism, and atherogenesis. Perhaps sulphur compounds act as inhibitors of essential enzymatic processes. Commenting on this possibility a recent editorial in the *British Medical Journal*³ suggests that not only CS₂ but sulphur dioxide, an important and prevalent atmospheric pollutant may also be atherogenic.

A study of the way in which these compounds might act could provide a clue to our understanding and prevention of CHD. Such research might be related to the present interest in the role of trace elements in this disease. One thing is clear:

there may be danger to the coronary arteries in the air we breathe.

L.H.N.

References

1. Tiller, J. R., Schilling, R. S. F. and Morris, J. N.: Occupational toxic factor in mortality from coronary heart disease. *Brit. Med. J.*, 4: 407, 1968.
2. Bruger, H. and Teisinger, J. (eds.), Toxicology of carbon disulphide. *Excerpta Med. Found. Monograph* 2, 1967.
3. Sulphur and heart disease. Editorial, *Brit. Med. J.*, 4: 405, Nov. 16, 1968.

On Earthquakes And Law Suits

At the end of March earthquakes were much in the news and this may well cause future embarrassment for the United States Atomic Energy Commission. First the Middle East suffered several tragic earthquakes. One in West Turkey March 28 killed fifty-three and rendered 10,000 homeless. One in Ethiopia on March 29 flattened the town of Serdo killing twenty-three and on March 31 activity at the north end of the Red sea caused damage in Egypt. A further severe tremor was reported along the south coast of Turkey on the same day. Is there a common factor. With our incomplete knowledge of what triggers off an earthquake nobody is likely to contradict absolutely the hint of such a common factor.

The second point about earthquakes comes from Dr. W. T. Pecora, the Director of the United States Geological Survey, who told a Senate committee considering the budget for earthquake prediction, that the survey predicted another massive earthquake in San Francisco certainly within the next thirty years and probably in the next decade. In the news headlines it was "San Francisco Quake inevitable within ten years." Whichever version one chooses it is certainly true that the San Andreas Fault which in some areas releases strain regularly in small earthquakes is ominously silent in certain other regions, one of them is San Francisco. In these quiet areas a vast amount of strain energy has accumulated.

The third point is that the multi-millionaire Howard Hughes told the USAEC that he would consider court action to stop any further underground nuclear tests that he considered unsafe. Mr. Hughes is not known as a pacifist. His concern is not primarily with the arms race, although if he were successful he could put a severe brake on the military plans. He owns a large amount of the Nevada desert and happens to be next door neighbor to the Pahute mesa portion of the test site. Like most neighbors he is very concerned lest the ac-

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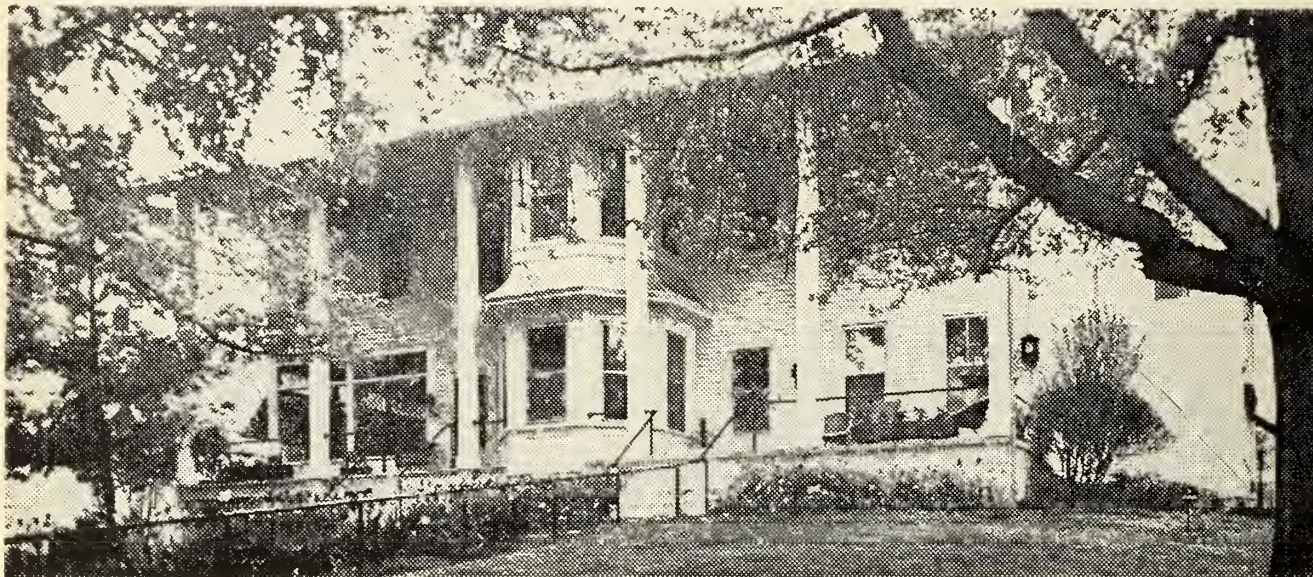
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tivities next door should spill over into his terrain and it is this that he fears at the moment.

The USAEC has had a tricky time finding suitable test-sites for its larger weapons. It is bound by treaty not to allow any fallout to cross a national frontier and so has had to avoid any region liable to fissuring. The effects of most underground weapons vary as the cube root of the yield and so safety required that once megaton tests were needed as offset to the previous testing of about 100 kilotons, the holes had to be twice as deep that is 5,000 feet. One of the advantages of the Nevada test-site so far has been the alluvium and tuff (a volcanic ash). Both are easy to drill through and act as very effective mufflers of the explosion. This is not true of the harder rocks deep in the Pahute mesa. Prediction of effects of explosion is much more difficult and according to Mr. Hughes' experts safety limit may now have been exceeded.

Other organizations in the past warned the USAEC of the dangers of testing but have been readily dismissed. So far the documentary evidence presented by the Hughes' organization have not been impressive. But there can be no doubt that Mr. Hughes is serious about this and if necessary will set up his own research team to advise on test dangers. Rocks have a way of misbehaving when under stress and it will soon become evident that there is no such thing as 100 per cent certainty.

Already it is known that large explosions on the test-site are causing local earthquakes. Not many of the details are publicized but last December a large test set off a series of sizeable earthquakes and no doubt many hundreds more were only detected by instruments close to the site. There is no reason to believe that this is the first time this has happened. So far all the triggered activity which is spread over several days has been very near the test-site itself. The Nevada test-site is prone to uninduced earthquakes as it is and the explosions doubtless act as strain relievers in some as yet unknown way.

It will not take long, however, for the public to become more than a little alarmed at the prospect of the San Andreas Fault being triggered (it is a good 300 km away). Seismologists would not take this suggestion very seriously, certainly less seriously than the possibilities of natural earthquakes triggering off others, an event known to happen sometimes. There does not seem to be much evidence that this triggering occurs on a scale approaching that in the Middle East. But if the newspapers regarded the Middle East events as part of a

pattern, so may San Franciscans and start looking in horror at the goings on in Nevada.

Perhaps Mr. Hughes will have started something. Eventually it seems inevitable that the USAEC must develop its test-sites on Amchitka Island far out in the Aleutians. One shot only has been fired so far but legal wrangles with USAEC by someone as determined as Mr. Hughes are usually noted for their length, cost and inconclusiveness. The first Aleutian test cost 11 million but subsequent tests cost less than half this figure and the USAEC may feel that the higher price is worth paying to keep neighbors happy.

Students of the arms race note that no amount of reason seems to have had the same eloquent effect on the nation as the 6,000 poisoned sheep in Utah, the missile site lowering the tone of suburbia and perhaps Mr. Hughes earthquake threatened real estate and the dread of the pacific coast being pushed into the sea.

L.H.N.

Reference

1. Bad Neighbors. *Nature*, 223, April 12, 1969.

Control Of Viral Infections: Host Resistance, The Interference Phenomenon

It has been known for over thirty years that infection with one virus may limit or exclude infection with a second unrelated virus. This is called the "Interference Phenomenon." Isaacs and Lindemann in 1957 showed that such activity was mediated by a protein of low molecular weight which they termed "interferon." It was produced by virus infected cells and protected new and uninfected cells from viral infection.

The importance of this discovery has become increasingly evident with the realization that the conventional antibody immune mechanism may have little to do with the early stages of recovery from viral infections. Interferon appears to provide the first line of defense being produced early in infection, functioning at the intracellular level to limit or to prevent viral infection. Once infected, however, the fate of the individual cell that is its life or death, appears to depend on factors other than antibody.

Originally the hope was that interferon might be produced in cells, purified and used to prevent or to treat viral diseases. There was great hope for the substance since it is active against essentially all viruses. The substance, however, is highly species-specific so that interferon produced in some species

is inactive against viruses infecting an individual of another species. Accordingly interferon for human use would have to be prepared in human cells. Exogenous interferon, however, has not achieved practical importance as a substance to be administered, first because there was no satisfactory source and second because the probable costs of preparation were so out of line with the estimated dose requirements as to be prohibitive.

The alternative approach was that of using some safe and effective inducing substance to stimulate the body to produce and distribute its own endogenous interferon. Many kinds of substances including bacteria, parasites, virus polysaccharides, mutagenic agents, antitoxin and the like may in fact stimulate the formation of interferon, but none so far are suitable for routine use because of toxicity, antigenicity, infectiousness and so on. At the Merck Laboratories, Hilleman and his group found that certain double strand RNA highly active in inducing interferon and host resistance in animals, cell cultures, and in conjunctiva against herpes. Such nucleic acid is not a normal component of cells but is comparable to that in the virus which provokes cells to make interferon.

Various double strand RNA have been found to induce interferon and to protect against virus infection. Some are synthetic of fungal or bacteriophage and of viral virion origin. The possibility of using these inducers in human and animal medicine is being actively explored. The interferon mechanism with its broad spectrum of antiviral activity gives hope for eventual prophylactic control of those viral infections in which the number of serotypes is so great as to preclude successful control by vaccines. Examples are the common cold caused by the numerous serotypes of rhinoviruses and the systemic and enteric diseases caused by enterovirus serotypes. Special situations might arise which might also call for use of these inducers for example pandemic influenza of a type for which there was no effective vaccine. Their use might also be of importance in preventing infection with lytic or oncogenic viruses in the early postnatal period of life prior to the development of immunologic capability.

Additionally effective interferon inducers might prevent the continuing re-infections which appears necessary to maintain the neoplastic state in RNA-virus dependent cancer as in leukemia. Only time will tell to what extent such utilization is practicable. It will, however, be necessary to work within the limits of the relatively short actions of inter-

feron and there will be need for continuing restimulation. What we do not know is whether this non-specific immune mechanism might not act like the autoallergic processes in cell and antibody mediated immunity and might cause adverse rather than beneficial effects. In such a case we might need to negate rather than promote the interferon effect.

There are some workers who consider the sequential administration of live viruses of low virulence to be a feasible but limited procedure for inducing host resistance by the non-specific interferon or interference mechanism. The Smorodentsefs have stated 1. that persons given appropriate live attenuated influenza virus vaccine by mouth were rendered resistant to respiratory illness from all causes for about two weeks. Similarly attenuated mumps vaccine given parenterally was said to afford some degree of protection against respiratory illness from all causes for at least two weeks, the longest period of observation.

Hilleman recently showed that live attenuated rubella virus vaccine given to young children may have afforded long-spectrum protection against naturally occurring respiratory illnesses, protection beginning as early as thirteen days after infection and lasting as long as three to four months.

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Analysis of 830 Cases of Rectal Adenocarcinoma

1. Progressively Improved Results of Treatment

W. H. Thomas, M. B., (England), R. A. Larson, M.D.,
H. K. Wright, M.D. and J. C. Cleveland, M.D.

Introduction

This study was undertaken to evaluate the results of treatment for adenocarcinoma of the rectum at the Yale-New Haven Medical Center as recorded in our Tumor Registry over the period 1931-60. Results were analyzed by decades to detect significant trends in presentation, diagnosis, therapy and results of therapy in this disease.

Analysis of Data

During the period 1931-60, there were 830 patients hospitalized at the Yale-New Haven Medical Center for adenocarcinoma of the rectum. In the first decade there were 177 cases; second decade, 297 cases and last decade 356 cases. There was 100% follow-up of all these patients.

Age

The youngest patient was 21 years old and the oldest 90. However, peak incidence for the disease occurred in the sixth, seventh and eighth decades of life.

Incidence by Sex

In the first decade there were 115 males and 62 females, a ratio of 1.85 (M/F). However, in the second decade, the ratio was reversed; 135 males and 162 females, M/F ratio of 0.89. This trend was accentuated in 1951-60 with 95 males and 261 females, a M/F ratio of 0.36. The total M/F ratio for the whole period was 0.71.

Prognosis Related to Time Interval From Onset of Symptom to Commencement of Therapy

Patients who presented as emergency situations requiring rather immediate operation with no previous history of symptoms were designated Time

“O”. Other groups were designated less than six months, six to twelve months and greater than twelve months. A five year survival for these groups showed that for patients in the Time “O” category, the survival rate was much poorer than in the other groups. A symptom interval of less than six months was accompanied by much better survival than in the other groups. After a symptom interval of more than six months, prognosis worsened, but never became hopeless even for patients with symptoms for more than a year.

Method of Presentation Related to Prognosis

Method of presentation denoted the predominant symptom leading to diagnosis. Blood loss, of all varieties, was termed bleeding. Obstruction, either acute, chronic, partial or complete was denoted as obstruction. Perforation denoted proven cases of perforation of the neoplasm or the bowel immediately adjacent to the neoplasm. A fourth category “other” covers all other manifestations at the time of presentation (such as complaints of alteration of bowel habit or backache, etc.). The outlook for patients presenting with perforation was bleak; the five-year survival in this series being nil in each decade. Patients presenting with obstruction also had a poor prognosis. The group labeled “other” is an intermediate group and the group presenting with hemorrhage had by far the best prognosis. Patients presenting with a complaint of hemorrhage only had an excellent five-year survival which was near 70% in the last decade.

End Results

These are shown in Table I. The operability rate progressively improved from 69% in the first decade to 87% in the last decade. This improve-

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* Abstract of an article accepted for publication by *Surgery, Gynecology and Obstetrics*.

Presented at The 21st Annual Winter Meeting of The Connecticut Society of American Board Surgeons, Wallingford, Connecticut, December 4, 1968.

TABLE 1

	1931-40	1941-50	1951-60
Total Cases	177	297	356
Operated	69%	73%	87%
Not Operated	31%	27%	13%
Operated for Palliation	17%	10%	22%
"Curative" Operation	52%	63%	65%
Operative Mortality	21%	5%	8%
Local Recurrence (% cases operated for cure)	6.5%	16%	13%
<i>Stage of Tumor (Duke's Classification)</i>			
Duke's A	30 (17%)	73 (25%)	96 (27%)
Duke's B	37 (20%)	84 (29%)	106 (30%)
Duke's C	110 (63%)	140 (46%)	154 (43%)
<i>Five-Year Survival Rates</i>			
Total	17%	21%	34%
Operated for Palliation	3%	3%	7%
Operated for Cure	30%	34%	46%
Duke's A	53%	67%	79%
Duke's B	22%	15%	25%
Duke's C	4.5%	2%	6%

ment was partially a result of a great percentage of tumors which proved to be Duke's A or B in the latter two decades and was also correlated with the fact that progressively more patients presented with bleeding early on in the course of the disease in each successive decade. In addition, progressive improvement in supportive measures allowed operation to be performed in elderly patients who would not have been considered fit for surgery in the 1930's and 1940's. Operative mortality was defined as death due to any cause within thirty days of operation. In the first decade it was 21%; by the last decade this had been reduced to 8%.

This group of patients does not include patients with carcinoma of the sigmoid colon. All of these patients had carcinoma of the rectum, most being at or below the peritoneal reflection. This was evidenced by the small number of patients who were able to have a sphincter-saving operation. In the entire series, only 38 patients had anterior resections and the rest, when operable, had abdomino-perineal resection.

The five-year survival rates improved progressively with each decade, but only reached 34% overall in the last decade. When rated by Duke's pathologic classification, the results showed little improvement in the Group B and C series. The marked change was in Group A cases where successive improvement occurred until the last decade when the five-year survival rate was 79%.

The local recurrence rate approximated 15% in the last two decades.

Comments

Only histologically proven cases of adenocarcinoma of the rectum were accepted in the study. The increasing number of cases seen in each decade is a reflection of the progressive increase in the bed capacity of the Medical Center. Whether or not the incidence of the disease is increasing was not determined. The change in sex ratio partially reflects the establishment of a nearby Veterans Hospital in 1951. However, it seems unlikely that this completely accounted for the total reversal of male to female ratio seen over this 30 year interval. It is probable that some real change in incidence related to sex is appearing. One of the striking findings of the study showed that in the last decade when patients presented for diagnosis and treatment with a symptom interval of less than two months, 87% survived five years. A comparison of this survival rate with the group of patients who presented with a primary complaint of bleeding argues heavily for increased patient education in the early detection of this cancer.

Our over-all results are quite comparable to a large series of patients (1,026) reported from the Cornell-New York Hospital by Glenn and McSherry.¹ Of 565 patients in that series operated with "curative intent", 40.5% survived five years. In the last decade of our study, the five-year survival for patients operated with "curative intent" was 46%. The local recurrence rate in our series also approximated the New York Hospital series.

Summary

The experience associated with carcinoma of the rectum over a 30 year period at the Yale-New Haven Medical Center has been analyzed. An over-all survival rate of 34% was achieved in the last decade. A 46% five-year survival rate was accomplished when resection was undertaken with curative intent. Analysis of method of presentation and symptom interval prior to surgery suggests that cancer of the rectum is highly curable early in the natural history of the disease. Advanced disease has a much poorer prognosis. Abdomino-perineal (Miles) resection has been the mainstay of curative therapy in this series. Further improvement in survival rates might be possible if patient and physician education aimed at early diagnosis became widespread, and successful.

Reference

1. Glenn, F. and McSherry, C. K.: *Carcinoma of Distal Large Bowel*. Amer. Surg. 163:838, 1966.

Cryosurgical Treatment of Tumors

John O'L. Nolan, M.D.

Modern cryogenic therapy began in 1960 with Cooper's exciting introduction of the cryo-probe for the treatment of intracranial lesions, but as long ago as 1900, A. Campbell White had successfully treated superficial skin lesions with liquid air applied with saturated cotton swabs. The successful production of closed cryo-probes and direct spray devices, has developed a wide number of uses for hypothermic necrosis and much of its great potential waits merely upon the imagination of the investigators. The Cryogenic effect is produced by the application of super-cooled liquids to living tissue for a period of time long enough to produce cellular necrosis by freezing. Thermo-couple control of an area can be maintained while tissue temperatures reach between twenty to thirty degrees below zero centigrade. Following the cryogenic application, the treated area may appear hyperemic and will weep for a short period, but after this, a relatively compact inert area of necrosis develops which is gradually sloughed off, leaving a clean smooth keratinized base. During this period, the patient has practically no clinical distress and, in fact, they all state that some minor pain may be present for a few hours and then disappears. The benign course following cryogenic treatment is due to the aseptic type of necrosis which is produced.

The cryogenic effect has many uses in the hands of the general surgeon. I have found it extremely useful in the primary treatment of large skin cancers, especially in the elderly, where excision would require grafting, possibly general anesthesia and hospitalization. It is of great value in treating multiple lesions, where numerous small incisions and sutures make a tedious procedure of something that can be done neatly with a few seconds of liquid nitrogen spray, and with a minimal deformity resulting. It has proved useful for technically inaccessible areas such as the ear or nose, where tight skin or folds make primary closure virtually impossible. It has been successful in treating recur-

rent or radioresistant skin carcinoma, and it has many applications in primary or palliative treatment of extensive intracavitary lesions. In this regard, it has been successfully used to treat several intraoral recurrences and to palliate a patient with an obstructing leiomyosarcoma of the rectum. This patient has now been free of clinical distress for a year after one treatment.

In treating patients, facial lesions have been locally anesthetized to avoid a startle reaction which might result in injury to the eyes or other areas. The eyes are protected with vaseline packs and 3M plastic drapes, but many superficial lesions in other areas require no anesthesia, and the patient senses only the nip of localized sleet storm. Successful treatment varies from fifteen seconds to as much as thirty minutes (for palliative relief of large necrotic recurrent tumor). One treatment is all that is usually needed. Repeated application in the same area can be accomplished safely, however, if such should be necessary. Narcotics have not been needed after treatment, and it has been observed that cryosurgery provides such relief for patients with extensive "terminal lesions" that the need for narcotics has been markedly reduced.

The cosmetic effect is very satisfactory and it has been my experience that the end result is very pleasing to the patient.

In breast surgery, it has an application in treating recurrent carcinoma in situ. Many of these recurrences are notably resistant to radiation. I have also used it as an adjunct to excisional surgery for diffuse carcinoma of the breast where the line of resection from the thoracic wall was not grossly distinct enough for one to be sure that a microscopically clean plane was left behind. In this instance, the entire area was frozen with nitrogen spray, and the mastectomy wound was closed with a drain left in the lower end. It healed well with a minimum of serious drainage and discomfort.

DR. JOHN O'L. NOLAN, Visiting Surgeon, St. Francis Hospital, Hartford.

Presented at The 21st Annual Winter Meeting of The Connecticut Society of American Board Surgeons, Wallingford, Connecticut, December 4, 1968.

Illustrative Case Report

The patient is an active 85 year old white woman with a three year history of a growth beginning at the anus and extending peripherally outward in triangular fashion for several centimeters (see illustration 1). Under local anesthesia and with thermocouple control, the lesion and an adequate margin was solidly frozen (illustration 2) and she was discharged from the hospital in 72 hours without any dressing, had no interference with bowel function, no medication for pain and the complete disappearance of the lesion is shown in illustration 3, ten weeks after treatment. She was hospitalized as a precautionary measure and because she lived alone. In the light of her trouble free postoperative state, I would not hesitate to treat a similar lesion on an outpatient basis. Excisional surgery with a graft or rotated flap procedure would have made this case a major problem, in contrast to the easily controllable situation it became with the liquid nitrogen spray.

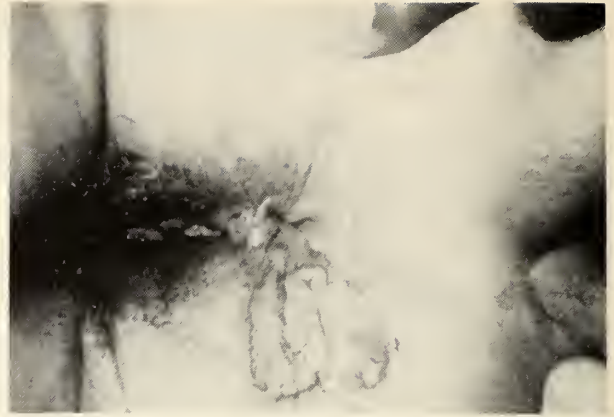


Figure 1
Lesion Before Treatment

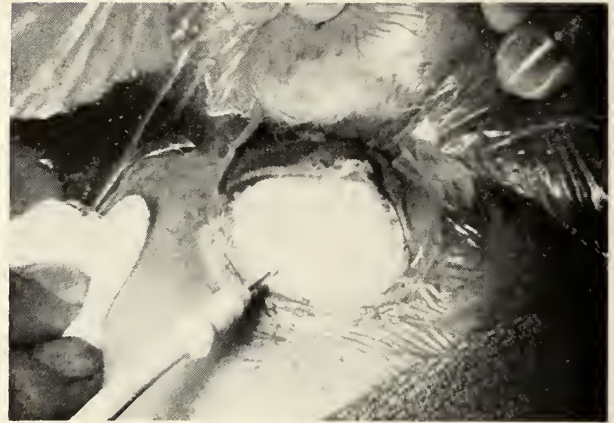


Figure 2
Actual Treatment Phase

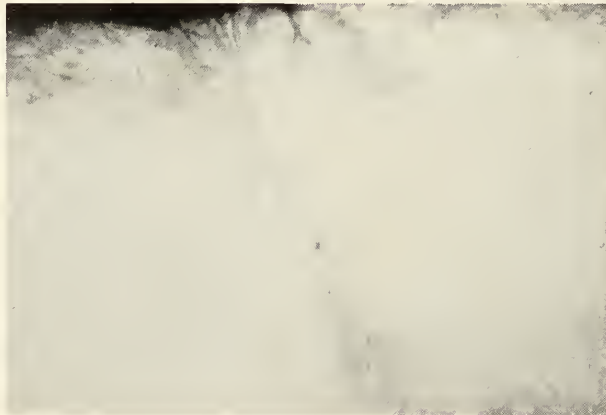


Figure 3
End Result

The Nature of Pancreatic Ascites

Timofey Kirianoff, M.D., Gerald O. Strauch, M.D. and
J. Forbes Rogers, M.D.

Since "common things occur commonly", as someone said, the surgeon confronted by a patient with ascites usually initially considers liver disease or malignancy as the cause. Occasionally, ascites has a more uncommon etiology. A massive intra-peritoneal collection of pancreatic juice, so-called pancreatic ascites, is one such unusual cause. Fifteen years ago, Smith¹ reported the first such case, and since that time a total of sixteen additional cases have been documented in the literature (Table 1). The following represents the eighteenth reported such case.

TABLE 1
REPORTED CASES OF PANCREATIC ASCITES

Date	Author	Number of Cases
1953	Smith ¹	2
1957	Hardy & Bowlin ²	1
1960	Gambill et al. ³	1
1962	Barua et al. ⁴	4
1962	Schmidt et al. ⁵	1
1966	MacLaren et al. ⁶	5
1967	Cameron et al. ⁷	1
1968	Parrish et al. ⁸	2
1968	Kirianoff et al.	1
TOTAL		18

Case Report

A forty-year-old Negro male was admitted to the Stamford Hospital on September 22, 1968, with the chief complaint of abdominal swelling of one week's duration, associated with a dry cough and difficulty in breathing. One month prior to admission he experienced abdominal pain and moderate abdominal swelling; this seemed to subside, but increased in severity one week prior to admission. He denied all other gastrointestinal symptoms, except for anorexia and a weight loss of thirty-five pounds over a period of eight months. He admitted to chronic alcoholism and had been hospitalized several times for this reason.

Physical examination revealed a poorly nourished Negro male with a grossly distended abdomen and evidence of ascites. Muscle wasting was evident, but the rest of the physical examination was unremarkable.

Admission laboratory data revealed a hemoglobin of 14.9 grams percent and a hematocrit of 45 percent. The white blood count was 8700 per cubic millimeter. Urinalysis was essentially normal. The serum electrolytes were within normal limits, except for a mild hypochloremia. The blood sugar was 120 milligrams percent, and the blood urea nitrogen was 8 milligrams percent. The total serum bilirubin was 0.5 milligrams; the serum glutamic oxalacetic transaminase, 24 units; the lactic dehydrogenase, 90 units; the alkaline phosphatase, 12 King-Armstrong units; the total serum protein, 5.0 grams percent, with an albumin of 3.1 grams percent. The bromsulfalein retention was 10 percent in 45 minutes. The prothrombin time was normal. Stool specimens were guaiac negative.

On admission a presumptive diagnosis of Laennec's cirrhosis with ascites was made. The patient was placed on a low salt diet; attempts at diuresis were unsuccessful.

Two days following admission, a diagnostic paracentesis was performed; serosanguineous fluid withdrawn failed to reveal evidence of tuberculosis, neoplasm, or bacteria. A second diagnostic tap two days later showed an amylase level of 20,000 Somogyi units. A third tap revealed an amylase level of 16,000 Somogyi units and a protein content of 3.6 grams percent. On this same day the serum amylase level was 724 Somogyi units.

These findings prompted further diagnostic evaluation. The serum calcium, phosphorus, and magnesium levels were found to be within normal limits. An intermediate strength PPD was negative. The chest X-ray was negative; contrast X-rays of the esophagus, stomach, small bowel, and colon revealed only evidence of edema of small bowel. A liver scan showed slightly spotty uptake, and the electrocardiogram was essentially normal.

A diagnosis of pancreatic ascites, probably secondary to pancreatic duct disruption, was made, and the patient underwent operation on his seventeenth hospital day. Prior to entering the peritoneal cavity, 5300 cubic centimeters of amber-colored ascitic fluid were slowly withdrawn through a trocar, the fluid subsequently showing an amylase concentration of 27,300 Somogyi units. The intraperitoneal organs were all found to be moderately edematous. The liver was normal in appearance. A small opening measuring approximately three millimeters in diameter was noted in the gastrohepatic ligament; through this aperture ascitic fluid was seen leaking into the free peritoneal cavity. Upon entering the lesser sac and elevating the stomach, a small pseudocyst of the pancreas measuring approximately three centimeters in diameter was discovered communicating with the main pancreatic duct, the roof of the cyst being the gastrohepatic ligament at the site of the perforation described above. The pancreatic duct at this point contained five small stones which were removed. A transgastric

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cystgastrostomy was performed for internal drainage of the pseudocyst. A liver biopsy which subsequently revealed chronic subcapsular and portal inflammation of the liver with slight fatty infiltration was performed.

In the post-operative period the serum amylase promptly returned to normal. The patient made a satisfactory recovery and was discharged on the twentieth post-operative day. He has since been seen as an outpatient where he reported a twenty pound weight gain; serum amylase was normal at that time.

Literature Review

We have reviewed the cases of pancreatic ascites reported in the world literature (Table 1). The largest series, that of MacLaren and associates,⁶ included complete data on only one of the five cases reported; all five patients had associated pseudocysts of the pancreas. Associated clinical findings are listed in Table 2.

TABLE 2

AGE, SEX, AND PREDISPOSING FACTORS IN PANCREATIC ASCITES

Case Number	Age	Sex	Alcoholism	Trauma	Pseudocyst
1	30	F	—	—	—
2	44	M	+	—	+
3	5	F	—	+	—
4	54	M	+	—	—
5	47	M	+	—	+
6	34	F	+	—	+
7	26	M	+	—	+
8	25	F	+	—	+
9	35	M	+	—	+
10	46	M	+	—	+
11	?	?	?	?	+
12	?	?	?	?	+
13	?	?	?	?	+
14	?	?	?	?	+
15	30	F	+	—	+
16	28	F	—	+	+
17	19	M	—	+	+
18	40	M	+	—	+
			10/14	3/14	15/18

TOTALS 18 Range: 8 M
5-54 Years 6 F

Symptoms and laboratory data are summarized in table 3 and 4.

Comment

The syndrome of pancreatic ascites is constituted by the presence of massive ascites, hyperamylasemia, and high concentrations of amylase and protein in the ascitic fluid. Because alcoholism is seen so commonly in association with pancreatic ascites, the patient with this syndrome may be easily mistaken for a cirrhotic with hepatic ascites. It is therefore important that surgeons be alert to this possibility when confronted by a patient with ascites. No diag-

TABLE 3

SYMPTOMS AND SIGNS IN PANCREATIC ASCITES

Symptom	Incidence
Abdominal swelling	14
Weight loss	11
Abdominal pain	10
Anorexia	10
Vomiting	6
Nausea	5
Ankle edema	4
Diarrhea	1
Fever	1

TABLE 4

CRITICAL LABORATORY DATA IN PANCREATIC ASCITES

Serum Amylase Levels	Number of Cases
Normal	1
Elevated	10
No data	7
Ascitic Fluid Amylase Levels	
Normal	0
Elevated	11
No data	7
Ascitic Fluid Protein Levels	
Data available	6
Range 2.9-5.7 grams per cent	

nostic importance can be given to the history, physical examination, or the gross appearance of the ascitic fluid. Of great diagnostic importance are the amylase concentration of the ascitic fluid, which has been high in all patients in whom the determination has been done, and the protein content of the ascitic fluid which has ranged from 2.9 grams percent to 5.7 grams percent (Table 4). In cirrhotic ascites, on the other hand, the ascitic fluid has a normal amylase level, and the protein concentration is usually less than 1.5 grams percent. Since the serum amylase may be elevated in about one fifth of cirrhotic patients,⁹ this determination, even though very helpful, may at times be equivocal. The underlying cause of this syndrome seems to be disruption of the pancreatic duct system with leakage of pancreatic juice into the free peritoneal cavity, as was demonstrated in our case. Although the true incidence of pancreatic ascites is unknown, it is probably more common than the few reported cases suggest.

Operation in the form of internal or external drainage has resulted in recovery in all cases. Reoperation was required in three cases which were initially drained externally^{1, 2, 8} because of persis-

tence or recurrence of a pseudocyst. The only additional complication recorded was that of homologous serum hepatitis in one patient. The only death was in a patient treated without operation.⁴

Summary

The syndrome of pancreatic ascites consists of 1) massive ascites, 2) hyperamylasemia, 3) high ascitic fluid amylase levels, and 4) high ascitic fluid protein levels in a patient with a known predisposing cause for pancreatitis. Since the sine qua non in the diagnosis seems to be a high ascitic fluid amylase, a plea is made for the determination of amylase in all ascitic fluid specimens, so that this syndrome will not be overlooked. In a patient in whom the syndrome of massive pancreatic ascites is present, internal drainage of the offending lesion seems to offer uniformly good results.

Addendum

Since the presentation of this paper, seven more cases of pancreatic ascites have been reported by Rosenberg et al.¹⁰ This series is the largest reported to date, bringing the total number of cases reported to twenty-five. As these seven cases represent thirteen percent of the total pseudocysts presented in Rosenberg's paper, it would seem apparent that pancreatic ascites has been a missed diagnosis in the past.

References

1. Smith, E. B.: Hemorrhagic Ascites and Hemothorax Associated with Benign Pancreatic Disease, *Archives of Surgery* 67:52-56, 1953.
2. Hardy, J. D., and Bowlin, J. W.: An Investigation of Some Complications of Pancreatic Disease: Illustrative Cases with Notes on Management, *Annals of Surgery* 145:848-856, 1957.
3. Gambill, E. E., Waltman, W., and Scanlon, P. W.: Chronic Relapsing Pancreatitis With Extensive Subacute Peritonitis and Chronic Recurrent Massive Chylous Ascites, *American Journal of Medicine* 28: 668-670, 1960.
4. Barua, R. L., Villa, F., and Steigmann, F.: Massive Ascites Due to Pancreatitis, *American Journal of Digestive Diseases* 7: 900-906, 1962.
5. Schmidt, E. H., and Whitehead, R. P.: Recurrent Ascites as an Unusual Complication of Chronic Pancreatitis, *Journal of American Medical Association* 180: 533-535, 1962.
6. MacLaren, I. F., Howard, J. M., and Jordan, G. L.: Ascites Associated With a Pseudocyst of the Pancreas, *Archives of Surgery* 93: 301-303, 1966.
7. Cameron, J. L., Anderson, R. P., and Zuidema, G. D.: Pancreatic Ascites, *Surgery Gynecology and Obstetrics* 125: 328-332, 1967.
8. Parrish, R. A., Humphries, A. L., and Moretz, W. H.: Massive Pancreatic Ascites, *Archives of Surgery* 96: 887-891, 1968.
9. Cummins, A. J., and Bockus, H. L.: Abnormal Serum Pancreatic Enzyme Values in Liver Disease, *Gastroenterology* 18: 527, 1951.
10. Rosenberg, I. K., Kahn, J. A., and Walt, A. J.: Surgical Experience with Pancreatic Pseudocysts, *American Journal of Surgery* 117: 11-17, 1969.

BOOK ON SCIENTIFIC WRITING.—Since 1963 the American Medical Association has organized and subsidized more than a dozen seminars in medical writing. These have ranged in length from one day to eight weeks, and have been attended by many dozens of physicians and medical students.

Between August 1967 and August 1968, Lester S. King, M.D., and Charles G. Roland, M.D., the AMA staff members responsible for the sessions, wrote a series of communications for *The Journal of the American Medical Association*. These works were derived from the experience gained conducting seminars; a total of 25 articles appeared, under titles such as "Monotony," "Jargon," "Verbs," and "Why Not 'I' and 'We'?"

Now the entire group of essays, with some additional material in an appendix, is available as a paperbound book, *Scientific Writing*. Anyone wishing to obtain a copy may do so by sending his check for \$1 (for 11 or more copies, 75 cents each) to the Order-Handling Unit, American Medical Association, 535 N. Dearborn St., Chicago 60610.

Abstract: Post-Vagotomy ECG Abnormalities

Gregory J. Gallivan, M.D., Howard Levine, M.D.
and Andrew J. Canzonetti, M.D.

Abstract

Although ischemic ECG changes have been reported in patients with gastroenterologic disturbances, metabolic disorders, and with subarachnoid hemorrhage, similar findings have not previously been reported in humans following transabdominal truncal vagotomy. In a prospective study of 86 vagotomized patients at New Britain General Hospital, clinical and electrocardiographic status, as well as serum enzymes were evaluated before and after surgery. Twenty-six patients (30%) sustained postoperative ECG changes of varying degrees unrelated to any preoperative abnormalities. Two patients (2%) exhibited moderate anterior lead T inversion with prolongation of the QT interval during the first postoperative week. In five cases (6%) there was a markedly prolonged QT interval with deep, broad T-wave inversion occurring in in-

ferior and anterior leads. These abnormalities began one to four days postoperatively, persisted for weeks and were unaccompanied by correlative enzyme rises or clinical phenomena. The five cases with "total heart involvement" had changes closely resembling those attributed to vagal stimulation secondary to subarachnoid hemorrhage without actual myocardial involvement.^{1, 2} The 8% incidence of serious ECG abnormalities significantly exceeds published postoperative data³ and strongly suggests the occurrence of a vagal cardiac event.

References

1. Cropp, G. J.; and Manning, G. W.: Electrocardiographic changes simulating myocardial ischemia and infarction associated with spontaneous intracranial hemorrhage, *Circulation*, 22: 25-38, 1960.
2. Manning, G. W.; Hall, G. E.; and Banting, F. G.: Vagus stimulation and the production of myocardial damage, *Canad. Med. Assoc. J.*, 37: 314-318, 1937.
3. Driscoll, A. C.; Hobika, J. H.; Etsten, B. E.; and Proger, S.: Myocardial infarction and other electrocardiographic changes in the postoperative period, *Bull. of Tufts-N.E. Med. Center*, 6: 1-7, 1960.

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Presented at The 21st Annual Winter Meeting of The Connecticut Society of American Board Surgeons, Wallingford, Connecticut, December 4, 1968.

Long Term Results of Operation For Sliding Esophageal Hiatus Hernia

Lewis A. Giffin, M.D.

Many operative techniques have been described for the repair of esophageal hiatus hernia. Although operative mortality has been low, the occurrence of symptoms suggestive of recurrence has been distressingly high after these procedures. Para-esophageal hiatus hernia is essentially a mechanical problem which is solvable by mechanical reduction of the herniated stomach and repair of the defect. With sliding esophageal hiatus hernia, however, in addition to the mechanical herniation, there is a functional defect which allows regurgitation of acid gastric contents into the distal esophagus. Pyloroplasty and vagotomy have been advocated for this condition by some surgeons who have felt that mechanical measures were not enough to insure against acid reflux.

The present study was undertaken to discover just how successful the several techniques of esophageal hiatus hernia repair in use at Hartford Hospital prior to 1966 were in alleviating symptoms, and to discover whether variations in technique influenced these results. Patients with para-esophageal hiatus hernia without symptoms of esophageal reflux were excluded from this review.

Material and Methods

During the nine year period between January 1958 and December 1966, 153 patients underwent operative repair for sliding esophageal hiatus hernia at Hartford Hospital. Four patients died postoperatively (2.6%), three patients died of unknown or unrelated causes long after hospital discharge, and 16 patients were lost to follow-up. An evaluation of the remaining 130 cases forms the basis of this report.

Diagnostic Criteria

All 130 patients had symptoms referable to their esophageal hiatus hernia prior to operation. The incidence of major symptoms is listed in Table I. Only one patient presented with bleeding without associated heartburn or dysphagia. Barium contrast radiographs demonstrated a hernia in every case and also revealed esophageal ulceration in four pa-

TABLE I

PREOPERATIVE SYMPTOMS—130 PATIENTS

Dysphagia	— 91 pts.—70%
Heart Burn	—115 pts.—96%
Bleeding	— 26 pts.—20%

tients, stricture in ten patients, inflammation in thirty-seven patients and reflux in twenty-two patients.

Esophagoscopy was done in thirty patients and documented one esophageal ulcer and two strictures.

Indications for Operations

Although 100% of the patients had symptoms referable to esophageal hiatus hernia which had not responded well to medical therapy, in 12 cases the primary indication for operation was gastroduodenal peptic ulcer, and in another 12 patients the primary indication for operation was disease of the biliary tract. In the remaining 106 patients peptic esophagitis was the primary reason for operation.

Operative Procedure

Many different techniques were used by the 37 surgeons who performed these operations. However, for purposes of this paper, I have arbitrarily classified the operations in three major headings;

1. Crus Closure only (CCO)—18 patients.
2. Sub-hiatal fixation (SHF)—112 patients.

In the SHF group crus closure was accompanied by any or all of the following maneuvers; suture of the esophagus to the hiatus, closure of the "angle of His", suture of the phrenicoesophageal ligament to the under surface of the diaphragm, gastric fundopexy, and/or gastrostomy.

3. Bilateral truncal vagotomy and gastric emptying procedure (VEP)—34 patients.

Seventy-three repairs were done through an abdominal incision, 51 through a left thoracotomy incision, and in six cases a combined thoracoabdominal approach was used. Most of the patients with

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thoracic incisions underwent an Allison type repair, usually with a counter incision in the diaphragm.

Follow-up Procedure

One hundred and thirty patients were contacted by personal interview or questionnaire. Subsequent hospital records, xray reports, and information from the attending physicians were reviewed when appropriate. The average period of follow-up was 44 months after operation with a range from 14 months to eight years. The patients were questioned about substernal pain or "heartburn", dysphagia, bleeding, pyrosis, nausea and vomiting. They were also asked to state whether they felt "improved", "no different", or "worse", after operation.

The result was evaluated as a "success" when the patient felt improved after operation and had no significant symptoms or signs referable to his hiatus hernia. A "failure" was determined by significant postoperative symptoms and/or a "no different" or "worse" overall evaluation. There were four improved "asymptomatic" patients with recurrence demonstrated by X-ray which were listed as "successes".

Results

Using rather strict criteria for "success" the overall rate of successful operative results was 78%. A summary of the operations used and results is presented in Table II.

TABLE II

SATISFACTORY LONG TERM RESULTS OF HIATUS HERNIORRHAPHY

	Without VEP		Totals
	CCO	SHF	
Thoracic Incision	—	39/49 (80%)	
Abdominal Incision	5/10 (50%)	28/35 (80%)	
Thoraco-abdominal Incision	—	2/2 (100%)	
Totals	5/10 (50%)	69/86 (80%)	
		74/96 (77%)	
	With VEP		Totals
	CCO	SHF	
Thoracic Incision	—	0/2 (0%)	39/51 (76%)
Abdominal Incision	8/8 (100%)	16/20 (80%)	31/51 (76%)
Thoraco-abdominal Incision	—	3/4 (75%)	5/6 (83%)
Totals	8/9 (100%)	19/26 (73%)	101/130 (78%)
		27/34 (80%)	

Numbers relate to number of patients, percentages relate to proportion with successful result.

VEP—Vagotomy plus emptying operation
CCO—Crus closure only
SHF—Subhiatal fixation

When the 24 patients with primary indications for operation of peptic ulcer or biliary tract disease are removed from this series, we are left with 106 patients who were treated primarily for their peptic esophagitis. Table III documents the results in these cases.

TABLE III

SATISFACTORY LONG TERM RESULTS OF HIATUS HERNIORRHAPHY
PEPTIC ESOPHAGITIS-PRIMARY INDICATION FOR OPERATION

	Without VEP		Totals
	CCO	SHF	
Thoracic Incision	—	39/49 (80%)	
Abdominal Incision	1/3 (33%)	24/30 (80%)	
Thoraco-abdominal Incision	—	2/2 (100%)	
Totals	1/3 (33%)	65/81 (80%)	
		66/84 (79%)	
	With VEP		Totals
	CCO	SHF	
Thoracic Incision	—	—	39/49 (80%)
Abdominal Incision	4/4 (100%)	11/15 (73%)	40/52 (77%)
Thoraco-abdominal Incision	—	3/3 (100%)	5/5 (100%)
Totals	4/4 (100%)	14/18 (78%)	84/106 (79%)
		18/22 (82%)	

Numbers relate to number of patients, percentages relate to proportion with successful result.

VEP—Vagotomy plus emptying operation
CCO—Crus closure only
SHF—Subhiatal fixation

Not all patients with postoperative symptoms had barium contrast films, but X-ray did prove anatomical recurrence of hernia from seven days to six years postoperatively in 12 patients, 8 of whom were symptomatic. Only three of the 8 symptomatic patients with anatomical recurrence by X-ray required reoperation and repair.

There were 29 patients whose result of operation was judged as unsatisfactory. Eleven patients with an Allison-type repair had symptoms of reflux esophagitis postoperatively, but in only three was there roentgenographic evidence of reflux or recurrent herniation. Three patients had advanced esophagitis with ulceration and/or stricture and required esophageal dilatation after operation. One patient had an untreated duodenal ulcer with pylorospasm which may have contributed to recurrence of the hiatus hernia.

Discussion

There is no statistically significant difference in the results of operation done by the thoracic approach when compared with operations done by the abdominal approach. The addition of vagotomy and pyloroplasty made no difference in the overall results. Even when the patients operated on primarily for ulcer or biliary disease were excluded, there still was no significant difference produced by the acid-lowering procedure (85% success with VEP and 80% success without VEP for patients operated primarily for esophagitis).

The results after various techniques of sub-hiatal fixation were not significantly different from each other or from the overall group to point to the superiority of one method over another.

One patient in five undergoing operative repair of symptomatic sliding esophageal hiatus hernia at Hartford Hospital from 1958 to 1966 had enough recurrent symptoms or signs to be classified as a "failure" from 14 months to eight years postoperatively. This high recurrence rate compares with reports from the Mayo Clinic (21%) and Iowa State University (28%), but seems too high to accept.

Minor variations in the techniques first recommended by Sweet and Allison have not effected the late results of operation, nor has the addition of vagotomy and pyloroplasty. No definite advantage of the various methods used for sub-hiatal fixation in this series of patients can be shown over crus closure alone.

These operations were done by 37 different surgeons, none of whom had a specific interest in surgery of hiatus hernia. Whether or not these results could be improved by closer attention to the technical details of operation is open to speculation.

In my opinion the superlative results recently reported by Belsey and Hill suggest that emphasis should be placed on maintaining a suitable length of intraabdominal esophagus with posterior fixation on the gastroesophageal junction. Time may prove that these newer concepts for restoring competency to the gastroesophageal sphincter are also inadequate, but something more is needed than crus closure with a few additional sutures to restore the angle of His. The addition of vagotomy and a

gastric emptying procedure may improve results of an inadequate anatomical operation, but probably is unnecessary if an adequate anatomical reconstruction can be accomplished.

Conclusions

1. A critical analysis of the late results of 130 operations for sliding esophageal hiatus hernia has shown that 22% of patients have recurrent symptoms from 14 months to eight years postoperatively.

2. There was no statistically significant difference in results between operations which were done by the abdominal or thoracic approach.

3. Although crus closure alone produced nearly as high a proportion of satisfactory results as did the procedure of crus closure plus some form of subhiatal fixation, our figures for crus closure alone are too few to be statistically significant. These results lead us to conclude that neither technique represents an adequate operation.

4. The addition of bilateral vagotomy and the gastric emptying procedure did not alter the results of operation unless there was an associated peptic ulcer.

5. On the basis of these poor results, a recommendation is made to change the technique of operation to incorporate the principles of posterior fixation and maintenance of a length of intraabdominal esophagus. Whether this change will produce better results remains to be seen.

Bibliography

1. Brintnall, E. S., Blome, R. A., Tidrick, R. T.: Late Results of Hiatus Hernia Repair. *Am. J. Surg.* 101:159-163, 1961.
2. Hugh, A. R., Ellis, F. H., Jr., Carlson, H. C. and Anderson, H. A.: Surgical Repair of Sliding Esophageal Hiatal Hernia. *Arch. Surg.* 91:228-232, 1965.
3. Sweet, R. H.: Experience with 500 Cases of Hiatus Hernia: a Statistical Survey. *J. Thorac. Cardio. Surg.* 44:145-152, 1952.
4. Allison, P. R.: Reflux Esophagitis, Sliding Hiatal Hernia and Anatomy of Repair. *Surg. Gynec. and Obstet.* 92:419, 1951.
5. Skinner, D. B. and Belsey, R. H. R.: Surgical Management of Esophageal Reflux and Hiatus Hernia: Long-term Results with 1,030 Patients. *J. Thorac. Cardio. Surg.* 53:33-50, 1967.
6. Hill, L. D.: An Effective Operation for Hiatal Hernia: an Eight Year Appraisal. *Ann. Surg.* 166:651, 1957.

THE PRESIDENT'S PAGE

Under the able chairmanship of Dr. John W. Norcross, Past President of the Massachusetts Medical Society, a meeting of the Organization of State Medical Association Presidents came to order on Saturday, July 12, 1969, at the Americana Hotel, New York City, immediately preceding the 118th Annual Convention of the AMA. Sixty-five presidents, presidents-elect and/or past presidents, representing thirty-five constituent State Medical Associations, were in attendance for the purpose of discussing persistent and new problems facing physicians in their attempts to deliver optimum care to the people of the United States. Following a brief business session, the audience was divided into four discussion groups or panels. The moderators of the panels presented summaries of the four groups' discussions to the entire assembly in the final hours of the meeting.

Emphasis was placed on both the successes and the failures experienced in trying to solve some of these problems at the state level, and recommendations were made for transmittal to practitioners across the country. In keeping with this objective, your president transmits to you the following food for thought:

Malpractice Insurance

Malpractice insurance is rapidly becoming a serious problem nationwide. Annual premiums are increasing markedly (in California, a neurosurgeon pays \$19,000 a year), and yet more and more insurance carriers are giving up professional liability coverage because of the high loss ratio. Several state medical societies are contemplating setting up group programs for their memberships; others are trying to improve the situation through state legislation; and still others have sought relief from their state supreme courts. At the moment, it appears that each state or region must try to find a solution to this problem at the local level.

Continuing Medical Education; Recertification for Licensure Overutilization and Title XIX Patients

There was general feeling expressed that, despite increased efforts by some states, there was some continuing overutilization in the delivery of medical care for Title XIX patients. Nothing short of intense effort by responsible physicians serving on Utilization and Review Committees, in each state will resolve this problem.

Osteopathy and State Medical Licensure Laws

The audience supported the AMA's position on Osteopathy and, in essence, emphasized the necessity of solving this problem at the state level with proper revision of State Medical Licensure Laws.

Other problems receiving serious consideration were: (1) distribution of physicians in rural areas, (2) Regional Medical Programs (RMP), (3) public relations and the "Public Image of Physicians", (4) medical students—SAMA vs. the more conservative vs the radical element, (5) the need for public speaking seminars, (6) adjudication of fees for medical care provided to Title XVIII and Title XIX patients, (7) what to do with the non-conforming physician, with due consideration given to his age, type of practice, location, and (8) methods to be considered to maintain high quality of medical care, especially in office practice.

The entire full-day program of the Organization of State Medical Association Presidents was truly instructive, comprehensive and open-minded. One could not help but feel proud of *our* accomplishments in solving some mutual problems. However, I felt quite humble with our failures in others. Characterizing the entire session was the great enthusiasm and energy shown by medical leaders of all states—in their attempt to continue to deliver good medical care to their patients despite federal intervention, excessive paper work, numerous meetings and our endless call upon the time of busy physicians.

STEVENS J. MARTIN, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

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SUMMARY OF ACTIONS COUNCIL MEETING Thursday, August 14, 1969

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Granoff, Weber, Jr., Edson, Brandon, Dean, Gardner, Fabro, Polivy, Rogol, Cramer, Harwood, Petrie, Roch, Grant, Nemoitin, Friedberg, McDonald, Pelz, Root, Jr., and von-Glahn. Also present were: Mrs. Lindquist, Mr. Donelan (AMA), Mr. Villano, Dr. Hess (Medical Director, State Welfare Dept.), Dr. Wiesel (President HCMA), Dr. Early, and Dr. Curtis.

Absent were: Drs. Abbot, Farrell, Wilson, Jr., Purnell, Johnson, Gorin, Palomba and Klare.

II. Introductions and Award Presentations

- (a) Benjamin Wiesel, Hartford, President of HCMA, was introduced and welcomed as a guest.
- (b) James H. Root, Jr., Waterbury, was introduced and welcomed as a new Associate Councilor from NHCMA.
- (c) Julius C. Early, Hartford, was presented with a CSMS Certificate of Service award in recognition of his outstanding contributions to the people and physicians of Connecticut as Director of the Red Cross Blood Program.
- (d) Charles P. Curtis, Jr., Fairfield, was presented with the AMA Certificate for Humanitarian Service award in recognition of his services to the people of South Vietnam, rendered under the AMA Volunteer Physicians for Vietnam Program.

III. Routine Business

Life Membership

It was VOTED to approve applications for Life Membership received from the following Active Members:

- Kirby S. Howlett, Jr., Milford (FCMA)—1970
- Lewis P. James, Hartford (HCMA)—1969
- Norbert Landecker, Bridgeport (FCMA)—1970
- John R. Lee, Southbury (NHCMA)—1969
- William J. Logan, New Haven (NHCMA)—1969
- Harry J. Wieler, Lakeville (LCMA)—1969

Date of Next Meeting

The date for the next Council meeting was set for Wednesday, September 10, 1969.

IV. Old, New and Special Business

Minutes of Meeting—CSMS-CG Liaison Committee

It was VOTED to accept as information copies of the minutes of the 4/28/69 meeting of the Liaison Committee with Connecticut General on Medicare B. Several recurrent questions were raised about CG's present payment policies and the Liaison Committee was requested to bring these up again at the next meeting of the Committee, scheduled for 8/18/69.

Communication—Connecticut Blue Cross

It was VOTED to accept as information a letter from Mr. Joseph F. Duplinski, CBC president, in which Mr. Duplinsky expressed appreciation for the Council's offer to furnish advisory personnel when Blue Cross begins to develop its program for prepayment of physicians' services (authorized by the 1969 General Assembly), and stated that CSMS would be kept informed "of any new developments as they occur."

Report of Delegate to Connecticut Hospital Association

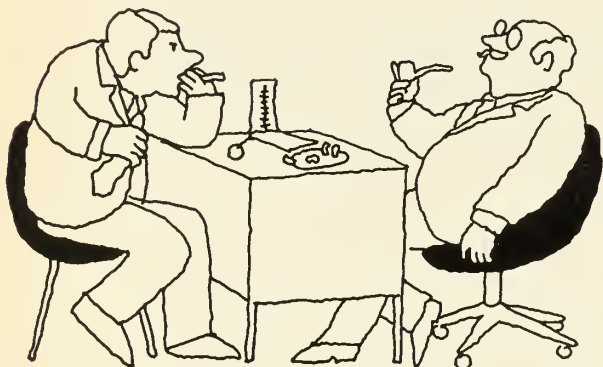
It was VOTED to accept as information, and with commendation, the report filed by Christie McLeod, Middletown, Chairman of the CSMS Committee on Hospitals, on her attendance at the 51st Annual Meeting of CHA (Hartford, 6/18/69) as delegate from the Society. There was some discussion of that section of the report which dealt with physician representation on hospital governing boards with respect to a report of the CHA Council on Professional Practice (not formally approved by CHA) which states: "Nothing . . . precludes membership of a physician on the Board if he meets all the qualifications for Trusteeship." Dr. Polivy felt that inquiry should be made by the CSMS Council as to what such "qualifications" were, and how they differed from the qualifications to be met by non-physician Board members.

Nominations to CRMP Technical Advisory Committees

It was VOTED to accept a report filed by the Ad Hoc Committee on CRMP TAC Nominations. The report listed qualified nominees for each of three

The Apprehensive Hypertensive

WELL, YOU HAVE WHAT WE CALL MODERATE HYPERTENSION—HIGH BLOOD PRESSURE. NOW I DON'T WANT YOU TO WORRY, BUT WE ARE GOING TO HAVE TO CHANGE A FEW LIVING HABITS. FIRST, WE'RE GOING TO HAVE TO CUT OUT SMOKING—ALTOGETHER.



THEN WE HAVE TO LOSE WEIGHT. 20 POUNDS SHOULD DO IT... WE'LL TALK A LITTLE LATER ABOUT THIS DIET WE'RE GOING TO START.



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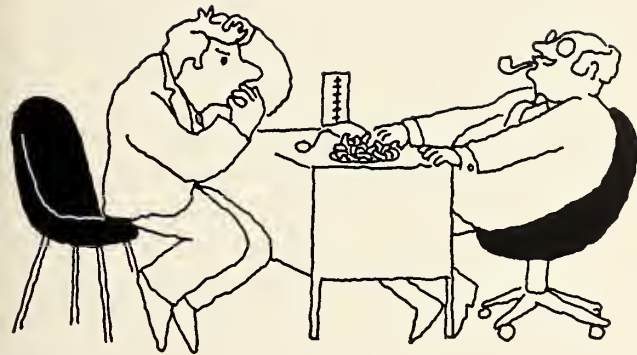
chlorthalidone 50 mg.
reserpine U.S.P. 0.25 mg.

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Indications: Hypertension. **Contraindications:** History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases. **Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small-bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue coated potassium-containing formulations immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. **Use in pregnancy:** Because chlorthalidone may cross the placental barrier and appear in cord blood and thiazides may appear in breast milk, this drug should be used with care in pregnant patients and nursing mothers. When used in women of childbearing age, the potential benefits of the drug should be weighed against the possible hazards to the fetus. Use of chlorthalidone may result in fetal or neonatal jaundice, thrombocytopenia, and possibly

other adverse reactions which have occurred in the adult. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated mothers. **Precautions:** Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use, if needed, anticholinergic or adrenergic drugs or other supportive measures as indicated. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated. Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, the drug should be discontinued and potassium supplements given, provided the patient does not have marked oliguria. Take particular care in cirrhosis or severe ischemic heart disease and in patients receiving

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PROBLEMS.




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corticosteroids, ACTH, or digitalis. Severe salt restriction is not recommended. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** The drug is generally well tolerated. The most frequent side effects are nausea, gastric irritation, vomiting, diarrhea, constipation, muscle cramps, headache, dizziness and acute gout. Other potential side effects include angina pectoris, anxiety, depression, bradycardia and ectopic cardiac rhythms (especially when used with digitalis), drowsiness, dull sensorium, hyperglycemia and glycosuria, hyperuricemia, lassitude, restlessness, transient myopia, impotence or dysuria, orthostatic hypotension which may be potentiated when chlorthalidone is combined with alcohol, barbiturates or narcotics, leukopenia, aplastic anemia, skin rashes, thrombocytopenia, agranulocytosis, nasal stuffiness, increased gastric secretions, nightmare, purpura, urticaria, ecchymosis, weakness, uveitis, optic atrophy and glaucoma, and pruritus. Eruptions and/or flushing of the skin, a reversible paralysis agitans-like syndrome, blurred vision, conjunctival injection, increased susceptibility to colds, dyspnea, weight

gain, decreased libido, dryness of the mouth, deafness, anorexia, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Jaundice, xanthopsia, paresthesia, photosensitization and necrotizing angitis are possible. **Average Dosage:** One tablet daily with breakfast. **Availability:** Pink, single-scored tablets in bottles of 100 and 1000. (B) 46-600-C

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TAC'S, as requested by CRMP. Following additional nominations from the floor, by closed written ballot it was VOTED to make nominations to CRMP as follows:

CUPISS Program: Marvin Garrell, Fairfield; Isadore H. Friedberg, Newington.

Coronary Care Training Program: Harold E. Speight, Middletown; Wallace B. Liebowitz, Bridgeport.

Regional Library Services Program: Louis H. Nalium, New Haven; Herbert Levine, Middletown.

Reports on Recent Medicaid Developments

- (a) It was VOTED to receive as information a letter from Commissioner George J. Conkling, Department of Finance and Control, informing the Council that his Department is not developing a new fee schedule for Medicaid at the present time, and that if and when such development is undertaken he "would be most pleased to work with the Connecticut State Medical Society".
- (b) It was VOTED to receive as information verbal reports by CSMS representatives who met with Welfare Commissioner and his staff in early July to ascertain what his plans were for the Medicaid program during the next biennium (policies, payment schedules, etc.) and what functions he would expect a "Medical Advisory Committee" to carry out in relation to same. Pursuant to this meeting, a letter was sent to the Commissioner by the CSMS Executive Director (7/24/69) which urged him to give full consideration to the new HEW regulations recently published in the *Federal Register* with a view toward developing a flexible payment schedule, and requested him to consult with the Attorney General to determine whether such a schedule would be permissible. A reply is being awaited.
- (c) It was VOTED to receive as information verbal reports from CSMS representatives (the same group as in (b) on a meeting which had been held on August 7, 1969, with Commissioner Shapiro and Commissioner Conkling to discuss the letter (to Commissioner Shapiro) which is described under (b) in the preceding paragraph. In brief, it can be said that the CSMS representatives were given little encouragement by Commissioner Conkling that a flexible payment schedule is possible under the existing Connecticut statutes and the General Assembly's failure to authorize the continuance or restoration of the "usual and customary charge" program. However, the two Commissioners agreed to seek the opinion of the Attorney General's office on this question and to apprise the Society promptly of same. Also discussed with the Commissioners was the problem associated with medical services being rendered to Medicaid patients in hospital emergency rooms as a consequence of the non-payment policy set by Commissioner Conkling earlier this year. Dr. Polivy reported that the Hospital Cost Commission recently reviewed this policy and has issued a new directive which will permit payment for physicians' services rendered in emergency rooms under certain conditions.
- (d) In response to a letter received from Orvan W. Hess, M.D., Welfare Medical Director, in which he apprised the Council of Commissioner Shapiro's desire that a Medical Advisory Committee be continued and function more or less in the same manner as the Title XIX MAC did during the trial year of "usual and customary charges", the Council voted to inform Dr. Hess that the Council will continue to study the question of whether a medical advisory committee would serve a useful purpose under a uniform fee schedule program; that the Council has requested its Liaison Committee with the Welfare Department to stand ready to receive any proposals as to a new payment schedule which the Commissioner of Welfare and/or of Finance and Control may find it possible to advance and to make recommendations to the Council concerning same; and that it is the Council's feeling that undue delay in relieving the uncertainty about the status of the Medicaid program which is widespread among physicians today will be detrimental to all parties interested in providing high quality medical care, under dignified circumstances, to the needy and near-needy in Connecticut.

Report—Committee on Public Relations

It was VOTED to act on a three-part report of the PR Committee as follows:

- (a) To approve a recommendation of the Committee that the Council "officially request all hospitals (in Connecticut) to provide (hospital-purchased) malpractice insurance for each physician serving without compensation on a hospital utilization review committee".
- (b) To approve a recommendation of the Committee that the Public Relations Director be authorized to contact the editors of national maga-

zines, at his discretion, for the purpose of seeking to interest them in publishing stories on Connecticut's Medicaid Program (1968-69), with particular emphasis being placed on the physicians' role in making the program effective and successful.

- (c) To approve a Committee recommendation that the Council "be encouraged to adopt its basic legislative goals now for introduction in the 1971 session of the General Assembly so that adequate time may be spent in acquainting the public, legislative leaders, opinion leaders and the Administration with their aims and purposes".

Progress Report—Ad Hoc Committee to Study Group Practice

It was VOTED to accept and approve a progress report filed by this Ad Hoc Committee, such actions covering the following matters:

- (a) With staff assistance, to seek to identify all "groups" practicing in Connecticut.
- (b) After identification, such groups are to be surveyed through the medium of an appropriate questionnaire.
- (c) For purposes of the proposed survey, the definition of a group shall be: A group of three or more physicians using common office facilities, using common diagnostic facilities and being in a professional financial partnership or corporation.

Report on CSMS-CRMP Liaison

It was VOTED to receive as information a "summary statement" of a joint dinner meeting (July 8, 1969) between CSMS officers and the Executive Committee of CRMP, which had been prepared by Henry T. Clark, Jr., M.D., CRMP Director. CSMS officers who had attended the meeting also commented verbally on the discussions held. In brief, it was reported that the purpose of the meeting had been to explore ways in which the Society might take a more active, cooperative part in supporting the implementation of CRMP programs among the CSMS membership and in encouraging physician participation in CSMS-approved programs at all levels. Since there was insufficient time to take up several other items on the agenda relating to CRMP at this meeting of the Council, no definitive action was taken on these reports and it was VOTED to table this item until the next meeting.

Report—Ad Hoc Committee on Annual Meeting Arrangements

It was VOTED to approve a recommendation of

the Ad Hoc Committee that there be a one-day format for the 1970 annual meeting of the CSMS House of Delegates.

The CSMS Charter requires that the County Medical Associations be notified "at least 60 days before each annual meeting so prescribed (by the Council or House of Delegates)". The Charter further requires that the County Associations hold their annual meetings "at least 20 days in advance of the annual meeting of the corporation (CSMS)" and that a list of the delegates elected at that meeting shall be sent to the Secretary (of CSMS) "at least 20 days before the date of such annual meeting". The CSMS Charter cannot be amended except by the Connecticut General Assembly.

Having accepted the opinion of the Ad Hoc Committee that mid-May was "too late" for annual meetings of CSMS, and that the latter part of April was greatly to be preferred, the Council VOTED to approve a proposal offered by the staff as follows:

- (1) That the Council establish the policy that the dates and places of the following year's annual meeting be set by the Council no later than its first meeting following the annual meeting each year, and that the component Associations be notified forthwith of the dates and place selected.
- (2) That, except when conflicts with other meetings or religious holidays are anticipated, the last week of the month of April regularly be given preference by the Council in setting the dates for the following year's annual meeting.
- (3) That the component Associations be requested to set the dates for their own annual meetings in conformance with this policy and with the Charter, and to amend their bylaws covering this matter if necessary.
- (4) That implementation of these policies be started in 1970 for the 1971 annual meeting.

Request for Advisors—Connecticut Ass'n. of Medical Assistants

In response to a request received from the president of the CAMA that the Council appoint four "advisors" to CAMA, it was VOTED to approve the request and to authorize the Chairman to select and appoint such advisors.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on August 14, 1969. Detailed minutes of the meeting are on file at 160 St. Ronan St., New Haven, for perusal by any interested member of the Society.*

Placement Opportunities

G.P. OR INTERNIST—for association with 2 other well-established physicians. Salary offered for first year, dependent upon experience and qualifications, then a partnership, if mutually agreeable. Fairfield County. New office building.

PEDIATRICIAN—Long-established mixed specialty clinic in Connecticut is seeking a fifth man for Pediatrics Department. Excellent salary opportunity. Two year trial before full partnership.

PHYSICIAN with wide knowledge of medicine and surgery wanted by casualty insurance company in Connecticut.

RADIOLOGIST—to associate with four radiologists; expanding hospital and office practice in Central Connecticut; remuneration negotiable leading to full partnership. Contact Albert C. Hurwit, M.D., 447 Connecticut Boulevard, East Hartford, Connecticut 06108.

G.P.—needed for community in Litchfield County. Community has a young, growing hospital, excellent public, as well as private schools within a short distance. Community is a mixture of farming, business and industry and has many summer residents, as well as permanent residents. There is also a great need for a Pediatrician and an Ophthalmologist. For further information, contact William J. Zehring, M.D., Chairman, Medical Procurement, Candlewood Lake Road, New Milford, Conn.

INTERNAL MEDICINE opportunity. East Hartford General Practitioner retiring from active practice limited to Adult Medicine. Ideal central location, Hamilton equipment. Fluoroscopy.

PRACTICE OPPORTUNITY FOR G.P. OR INTERNIST in upstate Connecticut at the foot of the Berkshire Hills. Office fully equipped available for rent because of death of physician. Located eight miles from excellent community hospital. Norfolk, Connecticut.

PHYSICIAN needed to practice in a rapidly expanding New England community of 45,000 (18,000 18 years and younger). Nine hospitals in immediate area. Between Springfield, Massachusetts and Hartford, Connecticut. Midway between Boston and New York. Sports, recreation, theatre, etc. are easily accessible. Contact C. S. Kissinger, Town Manager, Box 100, Enfield, Connecticut 06030.

PHYSICIAN for Emergency Room in 75 bed community hospital in northwestern Connecticut. Up to 40 hour week. Full cooperation from panel of

staff physicians who cover E.R. Room for remaining time. Must be eligible for Connecticut license. Full time service approx. \$30,000 annually. Reply: Robert L. McDonal, M.D., Roxbury Falls Road, Roxbury, Connecticut 06783.

SENIOR STAFF PSYCHIATRIST, full time, residential psychiatric rehabilitation center 40 miles from New York City, in desirable living area with good schools. Non-profit Foundation oriented to intensive, individualized, eclectic psychotherapy. Large out-patient service. Salary open, dependent on experience. Benefits include major medical insurance, life insurance and pension program. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Wanted

INTERNIST—34 years of age, Board certified with National Boards desires group or associate practice in Connecticut. Military obligations completed. Available immediately. Interest in practicing general Internal Medicine.

OBS-GYN—30 years of age, married, Board eligible with National Boards. Wishes to practice with an associate or on a sole basis in Connecticut. Available immediately Military obligations completed.

SURGEON—33 years of age, specialized training in vascular surgery, interested in an associate or small group type practice. Board certified with Connecticut license. Military obligations completed, available immediately.

ORTHOPEDECS—37 years of age, Board certified with National Boards desires partnership in Connecticut. Military obligations completed, available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

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In Memoriam

Dorian, George D., New Haven, Hahanamann 1939. Dr. Dorian practiced physical medicine and rehabilitation at St. Raphael's Hospital. He also served on the staff of the New Britain Memorial Hospital, Meriden Hospital, Mercy and Municipal Hospital in Springfield, Mass. Dr. Dorian was a member of the American College of Physical Medicine and Rehabilitation, National Rehabilitation Association, American Medical Association, Hartford County Medical Association and the Connecticut State Medical Society. Dr. Dorian died July 12 at the age of 58.

Gardner, Charles W., Fairfield, University of Maryland 1901. Dr. Gardner was a general practitioner in the Fairfield area for more than half a century. Born in Norwich, came to Bridgeport in 1906 and practiced medicine here until his retirement in 1965. Dr. Gardner had been a chief of medicine at Bridgeport Hospital, he was also on the staff at St. Vincent's Hospital. He was past president of the Bridgeport Medical Society and the Bridgeport Heart Association, former secretary of the Fairfield County Medical Association. Dr. Gardner was a member of the American Medical Association, Connecticut State Medical Society, Fairfield County Medical Association, American Heart Association and the New York Academy of Medicine. Dr. Gardner died July 6th at the age of 91.

Hall, Llewellyn, West Hartford, Harvard 1924. Dr. Hall was associated with the Phoenix Mutual Life Insurance Company. Dr. Hall was a member of the Board of Life Insurance Medicine, American Medical Association, Hartford County Medical Association and the Connecticut State Medical Society. Dr. Hall died June 21 at the age of 70.

Knauth, Marjorie, Wilton, P.S. Columbia 1923. Dr. Knauth was a general practitioner in Wilton area for many years. Dr. Knauth was a member of the American Medical Association, Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Knauth died July 30 at the age of 71.

O'Neill, John J., Bridgeport, Tufts College of Medicine 1932. Dr. O'Neill practiced medicine in this area for many years. He did postgraduate work in dermatology. He was on the staff of the Bridgeport and St. Vincent's Hospitals. He had been medical director at the Hillside and Englewood Hospitals.

Dr. O'Neill was a member of the American Medical Association, Connecticut State Medical Society and the Fairfield County Medical Association. Dr. O'Neill died July 6 at the age of 61.

Doctor's Office

Carl H. Braren, M.D., announces the opening of an office for the practice of internal medicine at Great Meadow Towers, 1800 Silas Deane Highway, Rocky Hill.

William G. Covey, M.D., announces his association with A. T. Licciardello, M.D. in the practice of internal medicine at 2875 Main Street, Stratford.

Raymond O. Craven, M.D., announces the opening of an office for the practice of urology at the Professional Building, Newtown-Danbury Road, (Route 6) Newtown.

Bennett I. Enowitch, M.D., announces the opening of an office for the practice of psychiatry at 60 Washington Street, Hartford.

Robert Flescher, M.D., announces the opening of an office for the practice of Internal Medicine and Gastroenterology at 21 Woodland Street, Hartford.

Kristaps J. Keggi, M.D., announces his association with Peter V. Dingman, M.D. and William H. Fisher, Jr., M.D. for the practice of Orthopaedic Surgery at 1211 West Main Street, Waterbury.

NEW BOOKS RECEIVED

Books received for review are acknowledged in this department and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers.

The Person: His Development Throughout the Life Cycle. Edited by Theodore Lidz. Basic Books, Publishers, 404 Park Avenue South, New York, New York 10016, 1968. 608 pp. \$10.00.

Hutchison's Clinical Methods, 15th Edition. Edited by Donald Hunter and R. R. Bomford. J. B. Lippincott Company, Philadelphia, 1969. 404 pp. \$7.00.

Abdominal Pain: A Guide to Rapid Diagnosis. Edited by Lars-Erik Gelin, M.D., Lloyd M. Nyhus, M.D. and Robert E. Condon, M.D. J. B. Lippincott Company, Philadelphia and Toronto, 1969. 128 pp., 26 figures and 7 tables. \$8.00.

Diagnostic Electrocardiography. Edited by Michael C. Ritota, M.D. J. B. Lippincott Company, Philadelphia and Toronto, 1969. 174 pp. 227 figures. \$15.00.

WOMAN'S AUXILIARY

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46th ANNUAL CONVENTION

WOMAN'S AUXILIARY TO THE AMERICAN MEDICAL ASSOCIATION

July 13-17, 1969 --:-- New York City

Speakers on safety, violence, and "Show and Tell" exhibits and films were among the outstanding features of the 46th annual convention of the Woman's Auxiliary to the American Medical Association. The meeting, held at New York's Waldorf-Astoria Hotel, July 13-17, attracted a registration of 919.

Auxiliary president, Mrs. John M. Chenault, Decatur, Ala., presided over the sessions. Mrs. Chenault filled the unexpired term of her predecessor, Mrs. C. C. Long, Ozark, Ark., who died suddenly on April 22.

A resolution on anti-violence in television and motion pictures, suggested by the Woman's Auxiliary to the Medical Society of the State of New York in memory of Mrs. C. C. Long, was accepted by the House of Delegates. The resolution stated:

WHEREAS, The Woman's Auxiliary to the American Medical Association is concerned with the health and welfare of this nation, particularly children and youth; and

WHEREAS, Television and motion picture programs, aimed both at adult and children audiences, depict acts of crime and excessive violence; and

WHEREAS, Such acts of violence may make children insensitive to brutality, may motivate them to imitate the sensationalism in this form of entertainment and may aggravate emotional instability and may produce indifference to human suffering; therefore be it

RESOLVED, That the Woman's Auxiliary to the American Medical Association go on record with a formal resolution in support of the already existing program of the National Auxiliary to curtail provocative violence on television and in motion pictures as recommended by our late National President, Mrs. C. C. Long, and be it further

RESOLVED, That constituent auxiliaries be encouraged to continue and strengthen campaigns for better programming in the television and motion picture industries.

The convention formally opened on Monday, July 14. Dwight L. Wilbur, M.D., 1968-69 AMA President, addressed Auxiliary members at the Monday luncheon honoring AMA Officers, Trustees and Wives.

During the luncheon, Mrs. Chenault presented the Auxiliary's contribution to the American Medical Association Education and Research Foundation to Milford O. Rouse, M.D., president of AMA-ERF. This year's record-breaking sum totaled \$428,875.77, bringing the Auxiliary's total contribution since 1951 to \$3,697,132.77.

In addition, a check for \$10,647 was presented by the National Auxiliary as a contribution to the Esther Long AMA-ERF Memorial Fund.

Ethel Alpenfels, Ph.D., Professor of Anthropology at New York University addressed the assembly at

They run a good chance of losing weight.

Exercise and Preludin run together in helping patients to lose weight.

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A few patients may experience overstimulation or insomnia. For a brief summary of all adverse reactions, precautions, warning and contraindications, please see the adjoining page.

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the Tuesday morning session. She predicted that in five to ten years society will require a physician who understands not only the physical and medical facts, but who understands the human being.

"The medical profession today must begin to examine attitudes, its own as well as its patients. To understand how a patient sees and how he acts is to understand the culture in which he lives," Dr. Alpenfels added.

The Tuesday morning session included presentation of the Emergency Health Services Award to the Woman's Auxiliary to the Honolulu County Medical Society for its outstanding achievements in alerting Hawaiian residents about various poisons.

A National Safety Council award was presented to the Woman's Auxiliary to the Oklahoma County Medical Society for its "Teen Sitter Workshop" program which trained more than 2,000 teenagers.

Following the award presentations, James Ray Adams, Ph.D., Associate Director for Safety Research, Continental Research Institute, discusses "Bending Elbows and Bending Twigs."

Some twenty exhibits, illustrative of the imaginative programs conducted by Auxiliary members, were on display Tuesday, July 15. This new "Show and Tell" feature allowed state and local auxiliaries to learn about one another's projects and provided an interchange of ideas. In addition, six films, developed by or for state and county auxiliaries, were shown.

Ann Landers, author of the world's most widely syndicated advice column, was the guest speaker at the Tuesday Luncheon honoring National Past Presidents, Officers, Directors and Committee Chairmen. Miss Landers cited some of the mail she receives from physicians' wives and mentioned some of their common problems.

"Lack of communication is the biggest problem of marriage today. The most common complaint of women today is that they don't have anyone to talk to," she added. The problem with teens today, she commented, is that "they have the disadvantage of having too many advantages." She said whereas their parents were teens during the depression and had to work hard just to survive, "the problem of teens today is how to get them off their behinds."

In her inaugural address, Wednesday, July 16, Mrs. Chenault outlined a plan for carrying out her theme for the year, "Active Leadership in Com-

munity Health With the Accent on Youth." She urged Auxiliary members to "study the health resources of the area in which they live and to evaluate the human resources with which they have to work." She added, "Let us direct our energy toward achieving better health conditions and to use our imagination in developing projects and programs which will meet the health needs of our communities."

Mrs. Chenault encouraged Auxiliary members to work closely with their husbands and sponsoring medical societies to "raise the level of health care for all the people." She added, as we work with our medical societies, let us always be ready to "stand up and be counted as we speak out with pride for those things that are *right* with American medical practice."

The Wednesday afternoon session concluded with a discussion on "Health Education Through Package Programs," followed by the showing of the film, "Escape to Nowhere." This film is the real life story of drug use told "like it is" by kids who use drugs. It is recommended for showing to senior high, college and adult audiences.

Mrs. Norman H. Gardner of East Hampton, Connecticut was elected and installed as constitutional secretary of the Woman's Auxiliary to the American Medical Association.

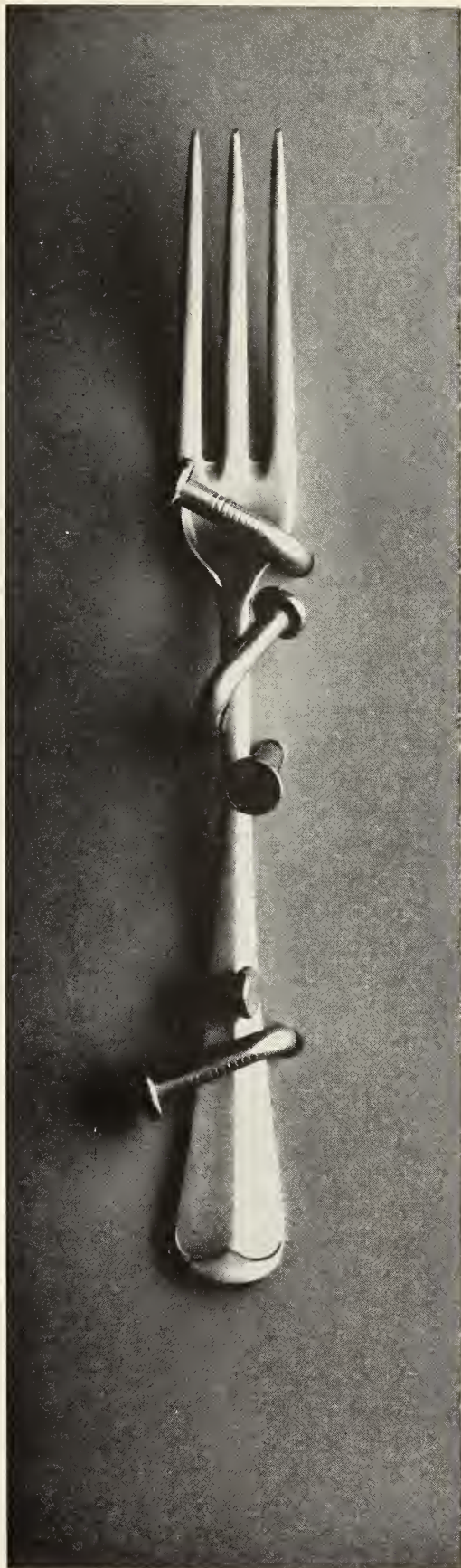
**First Annual
SIDNEY PERHAM
MEMORIAL LECTURE**

October 20, 1969

The first annual Sidney Perham Memorial Lecture will be held at the Hospital of St. Raphael, New Haven, Connecticut, Monday, October 20, 1969 at 5:30 p.m. in the Staff Assembly Room.

Dr. George Hammond of the Lahey Clinic Foundation, Boston, Massachusetts will be the guest speaker. The topic of the lecture is entitled, "Acromionectomy in the Treatment of the Painful Shoulder."

All interested Orthopedic Surgeons and other interested physicians are invited.



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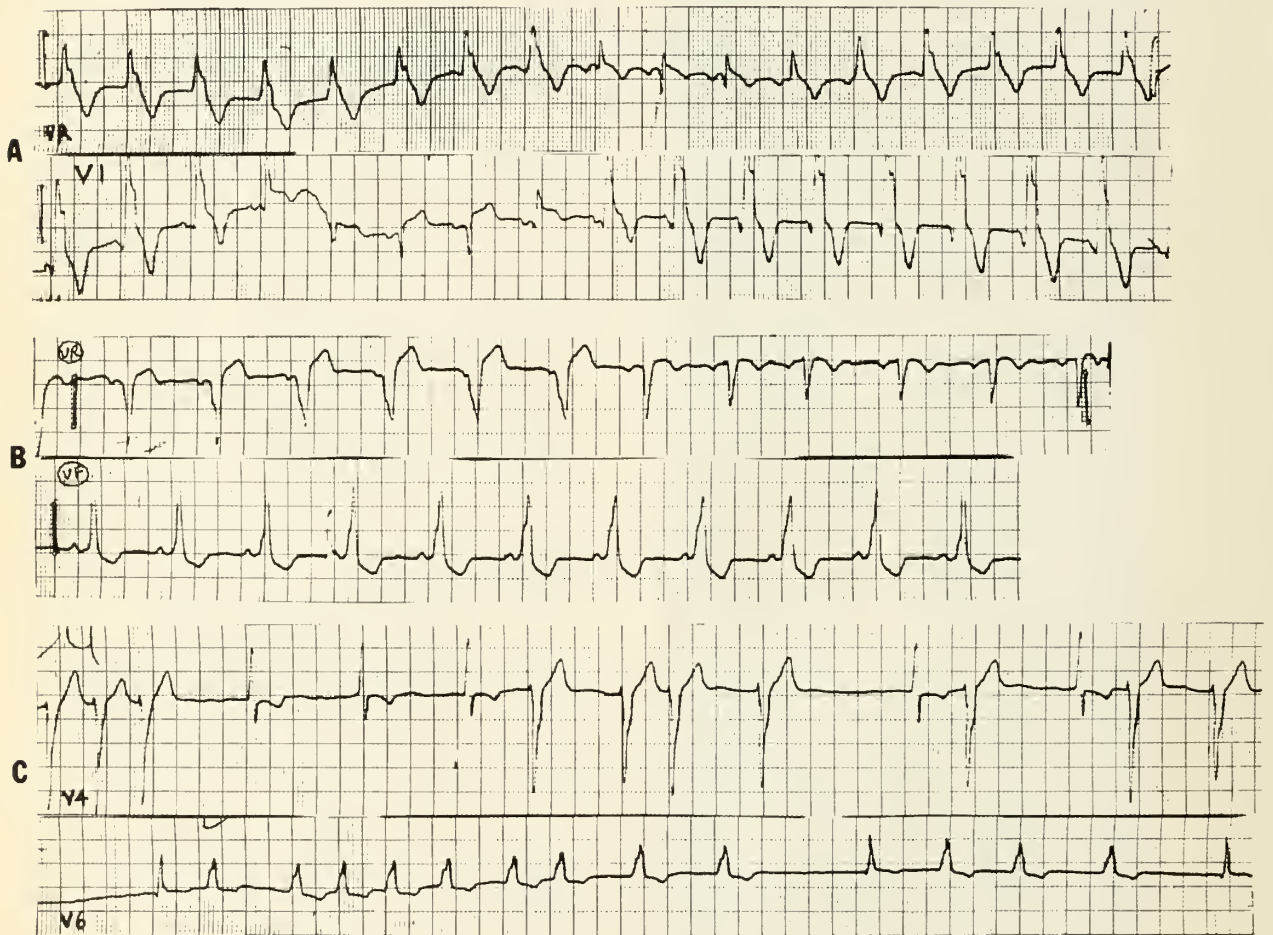
Yale-New Haven Hospital
New Haven, Connecticut

Prepared by
HYMAN M. CHERNOFF, M.D.
Associate Professor of Clinical Medicine,
Yale School of Medicine
Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

The rhythm strips mounted below were obtained from three different patients. In each instance the ventricular complexes exhibit both normal and prolonged I-V conduction times. The mechanism

responsible for the variation in I-V conduction time and QRS configuration is different in each patient.

Identify the three different mechanisms.



A—The rhythm is sinus with intermittent A-V dissociation. When the sinus is beating at a rate of about 110/min. the ventricles are under sinus control and the QRS complexes are of normal configuration and the I-V conduction time is normal. When the sinus rate slows to below 100/min., a pacemaker located in the ventricle assumes control of the ventricle (idio-ventricular tachycardia). This accounts for the abnormally wide QRS complexes which occur at rate of 100-105/min. Occasional fusion beats are noted during the transition back and forth from sinus to ventricular control of the ventricles.

B—The rhythm is sinus with rate of 80-88/min. The recurring periods of wide QRS complexes are due to the presence of intermittent Wolf-Parkinson White Phenomenon. As the degree of ventricular

pre-excitation increases the PR interval shortens and the delta waves increase in size and duration. The delta waves are negative in lead AVR and positive in lead AVF.

C—The rhythm is atrial fibrillation. The variation in QRS configuration and I-V conduction time is due to a rate dependent left-bundle-branch-block. When the diastolic pauses between successive ventricular beats exceed 0.92 sec. (calculated ventricular rate of 65/min.) the ventricular beats which follow such pauses exhibit normal I-V conduction time. When the ventricular response to the fibrillating atria is more rapid with diastolic pauses of less than 0.92 sec. (ventricular rate of over 65/min.) the ventricular beats exhibit the patterns of left bundle branch block.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

LOUIS H. NAHUM, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

CONNECTICUT PHYSICIANS ART EXHIBITION

The very talented Dr. John M. Freheit, had great enthusiasm and desire that this Connecticut Physicians Art Exhibition be continued, as a source of interest and focal point of attraction at the Connecticut State Medical Society annual meeting. During his critical illness many years ago I was honored to be asked by Dr. Freheit to continue as president to ensure its successful operation. Certainly, this is an excellent example of good cooperation between all concerned, to again bring such a show to a most successful conclusion. A list of the prize winners of this show follows.

Art Exhibit — Prizes 1969

Professional—Oil

- 1st Prize (8) Dr. Herman Austrian
154 Driftwood Lane
Trumbull, Conn.
- 2nd Prize (77) Dr. Louis M. Yavetz
184 Columbia Boulevard
Waterbury, Conn.
- Honorable Mention (85) Helen Wilson
19 East Town Street
Norwich, Conn.

Professional—Water Color

- 1st Prize (53) Esther McAlenney
Woodbridge, Conn.
- 2nd Prize (50) Dr. Donald Miller
236 Barbara Road
Middletown, Conn.
- Honorable Mention (49) Dr. Donald Miller
Middletown, Conn.

Professional—Mixed Media

- 1st Prize (82) Ruth Waskowitz
Kensington, Conn.
- 2nd Prize (24) Dr. Sophie Trent
96 Boylston Street
Meriden, Conn.

Professional—Sculpture

- 1st Prize (18) Sally Bradley Nelson
31 Stevens Street
Norwalk, Conn.

Children Paintings

- 1st Prize (28) Marian Holden
- 2nd Prize (3) John D. Murphy, Jr.
East Normandy Drive
West Hartford, Conn.
- Honorable Mention (45) Susan Harriet
Middletown, Conn.

Sculpture—Intermediate

- 1st Prize (14) Dr. Alan Dun
- 2nd Prize (79) Hazel H. Rentsch
61 Seymour Avenue
Derby, Conn.

Sculpture—Beginner

- 1st Prize (80) Patricia McDermott
35 Woodland Street
Bristol, Conn.
- 2nd Prize (42) Kurt Litter
16 High Ridge Road
West Hartford, Conn.
- Honorable Mention (15) Dr. Alan Dun
Hartford, Conn.

Beginners—Oil

- 1st Prize (36) Liliya P. Allison
Glastonbury, Conn.
- 2nd Prize (63) Elizabeth Fenney
West Hartford, Conn.
- Honorable Mention (62) Dr. Philip Fenney
West Hartford, Conn.

Intermediate—Oil

- 1st Prize (67) Dr. John Shull
Hartford, Conn.
- 2nd Prize (51) Dr. Paul McAlenney
Woodbridge, Conn.
- Honorable Mention (87) Dr. Richard Starr
Quaker Hill
New London, Conn.

Pastels, Water Color, and Collage

- 1st Prize (31) Dr. Stuart J. Danoff
Stamford, Conn.
- 2nd Prize (19) James Carroll Coyle
Orange, Conn.
- Honorable Mention (4) Anne Murphy
West Hartford, Conn.

Black & White—Etchings and Prints

- 1st Prize (74) Jon Schechtman
New Britain, Conn.
- 2nd Prize (48) Diane Harvey
Middletown, Conn.
- Honorable Mention (11) Dr. James Abel
New Britain, Conn.

Photography

- 1st Prize (26) Dr. Kurt Oster
Bridgeport, Conn.
- 2nd Prize (26) Dr. Kurt Oster
Bridgeport, Conn.
- Honorable Mention (33) Justin B. Gordon
West Hartford, Conn.

John M. Freiheit Award (to M.D.)

- (69) Dr. Tibor deCholnocky
Greenwich, Conn.

Best in Show

- (30) Dr. Stuart J. Danoff
Stamford, Conn.

Mrs. John Shoukimas, *Art Chairman*

A certain degree of "expertise" has helped smooth over many of the rough spots of previous exhibition arrangements. Unfortunately, a few of these rough spots remain. I enjoin the art hobbyests to carefully read the instructions mailed to them, and also appearing in *Connecticut Medicine*, prior to a future years show. Again, it must be said, that it is most difficult to single out certain persons or groups for special "thank yous," since the cooperation of so many made this possible. Not withstanding this however, accolades must be given to Mrs. John Shoukimas, and the Womans Auxiliary of the Connecticut State Medical Society. Their excellent support, which includes financial support, as well as the entire operation; from registration, through "hanging", supervision of the exhibit and "sign out". The State Society Office receives the thanks of all of us. Again, this is not only the financial support, but through the good offices of Mrs. Josephine Lindquist, the arrangements for the display and printing etc., were carried out excellently. The art committee itself, including Mrs. Carol Hess, Dr. and Mrs. Morrison, and Dr. and Mrs. E. Williams, Dr. Rightmyer, and many many others, all deserve special credit.

After several years of lying dormant, it gives me particular pleasure to have helped make this such a pleasing part of the annual meeting of our State Society. It is with regret, therefore, that I am announcing my resignation from this post. With the aid of any members of the Society, and especially of the Art Committee, we shall seek a new president. I will be most happy to continue helping this committee in whatever way, but have become increasingly aware of the fact that I cannot properly carry out other duties at the time of this art show, while serving as its president. Many many thanks to the many people who have worked with me in this endeavor.

STEWART J. PETRIE, M.D., *President*
Connecticut Physicians Art Exhibition

Cancer Linked To Immunity

(*Scientific Research*, 4: 18, March 31, 1969.)

Patients with Burton's syndrome — an immunological deficiency are more susceptible than the general population to lymphatic leukemia. Such patients lack plasma cells and normal mechanisms for producing antibody molecules. Such patients do not develop delayed-allergy and cannot reject homografts. After a prolonged period of immunological deficiency Good and Finstad¹ found these patients to develop lymph sarcoma, reticulum cell sarcoma, lymphatic leukemia, Hodgkin's disease or stomach cancer.

Children with ataxia-telangiectasia who constitute another group suffering from an immunological deficiency also develop cancer much more frequently than can be explained by chance. Such children lack many immunoglobulins, are poor antibody producers and reject homografts poorly. Their thymus glands show features of the underdeveloped embryonic type, the gland is an essential component of the antibody-producing system. Good and Finstad also pointed to the fact that the incidence of cancer increases and immunologic vigor declines with age.

They noted also that all known immunosuppressive agents although not carcinogenic themselves increase susceptibility to cancer. In humans as well as animals effective immunosuppression increases the chances of success in transplantation surgery but it has been found that the more effective the immunosuppression the greater the hazard of cancer. It was further suggested that all carcinogens may in fact also be immunosuppressive agents.—L.H.N.

Aflatoxin And Cancer

(*Scientific Research*, 4: 17, March 31, 1969.)

Sinnhuber, Wales and Lee¹ found that rainbow trout developed liver cancer after being fed moldy cottonseed meal and isolated from it the exciting agent aflatoxin which is produced by certain strains of the common mold *aspergillus flavus* which happened to be growing in the meal.

The team put 1,000 trout on a diet containing aflatoxin and found that "trout fed a diet containing just a few parts per billion of the aflatoxin contract liver cancer within only four months." It should be noted that the incidence of liver cancer in humans is highest in those areas of the world where moldy foods are common.

Of the four existing aflatoxins B₁, B₂, G₁, G₂, it is the B₁ that is the most carcinogenic. Aflatoxin had been found earlier in peanut meal and was connected with the deaths of thousands of turkey poults a few years ago.

Trout, however, are an ideal experimental animal as compared with rats. They develop cancers very rapidly and can be bred quickly and inexpensively in large numbers. Even more importantly they are very sensitive to carcinogens, and will develop tumors from doses only about one-hundredth as strong as those required to produce tumors in rats. Also rainbow trout don't need elaborate facilities for their care.—L.H.N.

Oral Fluoride Added To Bone Cancer Therapy

(*JAMA*, 208: 953, May 12, 1969.) Fluoride in 50–100 mg. daily is being given to a series of patients with cancers of breast and lung and prostate that have a predilection for metastasizing to bone.

In 31 of 75 such patients there was a good response. Bone pain was relieved in three to four weeks after starting fluoride. Most patients also received radiation therapy. The addition of fluoride seemed to increase bone deposition in one-third of the irradiated bones. Thirty patients did not respond.

There was no direct effect upon the neoplastic process or survival. However, the fluorine binds with calcium on bone surfaces, less calcium is lost, the bone becomes harder and more durable and the interface between the bone and cancer appears to decrease or slow down bone invasion.

Occasionally a patient developed nausea and emesis. It also cannot be given in renal insufficiency because fluorine is excreted within three hours of ingestion.—L.H.N.

Platelet Preservation

(*New England Jr. Med.*, 280: 1094, May 15, 1969.)

Dr. Scott Murphy and Frank H. Gardner report that the use of cold temperatures in the preservation of platelets should be abandoned. They found that standard refrigerated storage at 4° C. resulted in a marked shortening of the life-span of platelets.

Storage at ambient room temperatures (22° C.) however preserved a normal platelet life-span. Platelets stored at this higher temperature should be adequate for transfusion purposes for as long as 96 hours.—L.H.N.

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Scientists Boycott Potato Company

(*Scientific Research*, 4: 21, May 12, 1969.) A 200 member association of biologists in Maine has launched a boycott against F. H. Vahlsing Company, a potato processing concern in Maine because it is the principal polluter of a stream near the Main-Canada border with its plant in Easton, Maine. Robert Chute, the coordinator of the boycott thinks that if they succeeded here they will go after bigger game in the future.

"Scientists have a particular responsibility to do something about pollution because we are aware of the consequences of failing to take action in the past" Chute added. In this way the image of the conservation movement will be changed from "a layman's movement based on aesthetics to a scientifically based movement that stresses conservation for the sake of human survival."

"The one way to get tougher laws is to show the politicians and businessmen that the people's patience is wearing thin." It is hoped Dr. Chute is aware that "tough laws" administered by agents of the polluters will not solve the problem.—L.H.N.

Anticonvulsant Accelerates Drug Breakdown In Animals

(*JAMA*, 208: 784, May 5, 1969.) Diphenylhydantoin (Dilantin) increases drug metabolism in newborn rats. This suggests that a similar effect might be achieved in human infant's drug metabolism. Diphenylhydantoin's effects on drug metabolizing enzymes were studied by injecting newborn rats for three days prior to enzymatic assays.

In vitro studies of the treated animal livers were performed because it is the liver which contains most of the drug metabolizing enzymes. Diphenylhydantoin stimulated drug metabolism in rats studied at five to ten days of age. In some cases the drug increased newborn metabolism to adult levels. Experiments on adult rats showed similar increased activity of their drug metabolizing pathways. Since it is commonly combined with other drugs in therapy its stimulatory effect on drug metabolism may greatly influence the metabolism and activity of these other drugs.—L.H.N.

Carotid Flow May Predict Strokes

(*Kindt, G. W., Youmans, J. R. and Conway, L. W.:* *JAMA*, 208: 780, 1969.) Dr. Kindt describes a simple painless method of determining blood flow through the carotid arteries. The patient inhales 5-7 per cent CO₂ oxygen for 3 minutes and an ultrasound technique records blood flow velocity in the artery. The method causes no discomfort to

the patient who lies motionless on a stretcher. Twenty normal subjects increased their common carotid flow, an average of 48 per cent when the inspired gases was changed from pure oxygen to 5 or 7 per cent CO₂ in oxygen.

Five patients with advanced cerebrovascular occlusive disease had little or no response. This then is a way of identifying the asymptomatic person likely to have an ischemic cerebrovascular accident.—L.H.N.

Early Persistent Arrhythmias Correctable Without Drugs?

(*JAMA*, 208: 1278, 1969.) Drug therapy alone should not be used to treat arrhythmias but should be supplemented by attempts to normalize carbon dioxide, oxygen tension and electrolytes. Ayres found serious arrhythmias both atrial and ventricular in nine patients in whom conventional therapy with antiarrhythmic drugs and precordial countershock was ineffective. However, when their underlying metabolic derangements were corrected the arrhythmias promptly disappeared spontaneously.

Hypoxemia, and alkalosis combined appeared to be particularly arrhythmogenic as did hypokalemia.—L.H.N.

Biopsy And Prognosis Of Malignant Melanoma

(*Ervin Epstein, Kay Bragg and George Linden:* *JAMA*, 208: 1369, May 26, 1969.) Of 559 patients with black lesions on the skin 98 per cent were not melanomas and 2 were. In 31 suspected of melanoma, the diagnosis by histopathologic examination was proved in only 12.

Since melanoma surgery is mutilating, biopsy studies would be helpful provided they were not damaging to the patient. The authors compared survival rates of 115 patients on whom biopsies were done with those of 55 patients on whom definitive surgery was performed immediately. There was no evidence to indicate that incomplete removal of a malignant melanoma followed by definitive surgery even one week later decreases the probability of survival. They conclude, therefore, that biopsy studies are advisable in such cases before the institution of procedures hoped to be curative.—L.H.N.

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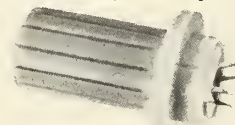
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U.N. Experts Report On C.B.W.

(*Elinor Langer: Science*, 165: 163, July 11, 1969.)

The much anticipated United Nations Report on Chemical and Biological warfare was released recently. It urged United Nations members "(1) to review the appeal to all states to accede to the Geneva protocol of 1925; (2) to make a clear affirmation that the prohibition contained in the Geneva protocol applied to the use in war of all chemical bacteriological and biological agents (including tear gas and other harassing agents) which now exist or which may be developed in the future; (3) to call upon all countries to reach agreement to halt the development, production and stock piling of all chemical and bacteriological (biological) agents for purposes of war and to achieve their effective elimination from the arsenal of weapons."

Langer points out that "our actions in Vietnam have clearly violated the spirit if not perhaps the letter of past international understanding on this point. We have already used 7,000 tons of C.S. (tear gas) in Vietnam."

The general conclusion of the report can thus be summed up in a few lines. "Were these weapons ever to be used on large scale in a war. No one could predict how enduring the effects could be and how they would affect the structure of society and the environment in which we live. This overriding danger would apply as much to the country which initiated the use of these weapons as to the one which had been attacked. . . . a particular danger also derives from the fact that any country could develop or acquire in one way or another a capability in this type of warfare. . . . The danger of the proliferation of this class of weapons applies as much to the developing as it does to developed countries." . . . Their use which could cause an enormous loss of human life has already been condemned and prohibited by international agreements in particular the Geneva protocol of 1925.—L.H.N.

Does Illness Cause Crashes

(*JAMA*, 208: 2257, June 23, 1969.) Disease is apparently not an important factor in causing fatal traffic accidents stated Dr. Susan P. Baker who studied autopsy records of 327 accident victims in Baltimore. Evidence of disease was found with similar frequency in drivers believed to have been responsible for their fatal collisions and in those who were not responsible.

At least 23 per cent of drivers over 50 "succumb to injuries which younger drivers would survive."

The percentage of drivers who had been drinking began to decrease in men after the age 40.—L.H.N.

New Products Parade

(*New Eng. J. Med.*, 280: 1074, May 8, 1969) In 1968 five new single drugs and two biologicals of considerable promise were accepted and put on the market:

(a) an agent to aid in the control of melanoma and chronic myelocytic leukemia.

(b) a product of value in arrhythmias and pheochromocytoma (propranolol).

(c) an adjunct for the prevention of rejection in renal homotransplants A.L.G. (tegretol)

(d) an anticonvulsant effective in trigeminal neuralgia (carbamazepine)

(e) an antidote for acute iron intoxication especially in children (dexyferamine)

(f) an antihemophilic factor and

(g) a substance for the prevention of the formation of active antibodies in the Rh neg. mother who has delivered an RH positive child (RH gamma globulin).—L.H.N.

Hippocratic Oath Remains Most Used Pledge For New M.D.'s

(*JAMA*, 209: 20, July 7, 1969) Preliminary results from all 85 four-year medical schools in the United States indicate that 92 per cent of these institutions used some type of oath, said Dr. R. S. Cranshaw. One-fifth used the classical form of the Hippocratic Oath. Thirty per cent administered a modified version rather than the original. The Hippocratic Oath has met criticism simply because its language and ideas originated twenty-four centuries ago, and on campuses today there is demand for relevance to the modern world.

Accordingly medical students and professors turned instead to the Declaration of Geneva drafted and adopted in 1948 by the Second General Assembly of the World Medical Association. In clear language it unmistakably dedicates the physician to serve in the best interest of the patient and in the service of humanity. Portions of the ancient oath sound foolish in the context of modern medicine and have been excluded and political and social considerations which are relevant today have been included.—(Nahum, L. H.: *A Definition Of Death: Ethical And Legal Questions Posed By Recent Advances In Medicine*. Conn. Med., 32: 779, November 1968).

The Choice And Uses Of Tetracycline Drugs

Of the many tetracycline drugs, tetracycline hydrochloride, tetracycline phosphate complex, chlorotetracycline (Aureomycin), and oxytetracycline (Terramycin) are available in both oral and parenteral formulations; tetracycline base, demeclocycline (Declomycin), methacycline (Randomycin), and doxycycline (Vibramycin) only for oral use; and rolitetracycline (Syntetrin) only for parenteral use.

Although the tetracyclines are mainly bacteriostatic, they are drugs of first choice in infections caused by *Vibrio cholerae*, *Rickettsia*, agents of psittacosis and lymphogranuloma venereum, the virus of inclusion conjunctivitis, and in a few other infections caused by susceptible organisms (Medical Letter, "The Choice of Systemic Antimicrobial Drugs," Issue 254, Oct. 4, 1968). Tetracyclines are not the drugs of choice in infections by many enterobacteria because of the increasing resistance of many strains of these bacteria.

DOSAGE — The antibacterial spectrum and *in vitro* susceptibility of organisms is essentially the same for all of the tetracyclines, and organisms resistant to one tetracycline are generally resistant to the others. It has not been shown that resistance develops more rapidly with some tetracyclines than with others. The dosages and frequency of administration of the various tetracyclines vary with rate of excretion, protein binding, and half-life; at recommended dosages and frequency of administration, the different tetracyclines have similar clinical effectiveness. The slower rate of excretion and the longer half-lives of demeclocycline (12 hours compared with nine hours for tetracycline hydrochloride), methacycline (15 hours), and doxycycline (20 hours) permit a reduction in dosage and in frequency of administration of these tetracyclines. In patients with renal insufficiency, however, a rapidly excreted tetracycline, such as tetracycline hydrochloride, should be used; after the usual initial dose, subsequent doses should be lowered to reduce toxicity.

ADMINISTRATION — The absorption of all oral tetracyclines is impaired when they are taken along with milk products or drugs containing calcium, magnesium, or aluminum, with the absorption of doxycycline least impaired. If the tetracyclines cause nausea or vomiting, however, they may be taken with small amounts of foods other than milk products.

In severe infections, intravenous administration is usually desirable for initial treatment (one to three days or more). Vomiting or malabsorption may also necessitate parenteral administration. Most intramuscular formulations of the tetracyclines contain lidocaine or procaine to minimize pain, but administration may still be painful and, furthermore, the drug may be poorly absorbed from the muscles. Most Medical Letter consultants do not recommend intramuscular use of any tetracycline.

ADVERSE EFFECTS — Adverse effects of the different tetracyclines are dose-related, and similar in kind, frequency, and severity. (See The Medical Letter, Vol. 10, p. 76, 1968 for a summary of adverse effects of tetracyclines.) Intestinal symptoms may not only be due to irritation of the gastrointestinal tract but also to overgrowth of resistant strains of *Klebsiella* and other organisms. The fixed-ratio combinations of a tetracycline and nystatin (as in Achrostatin V; and others) or amphotericin B (as in Mysteclin F) may reduce the number of *Candida* organisms in the stool but they have not been shown to prevent intestinal infection by *Candida*.

Intravenous tetracyclines should not be administered in a dose of more than 2 Gm the first day, or more than 1 Gm daily thereafter because of the risk of severe liver injury. Hepatic damage is especially likely to occur in pregnant women or in patients with impaired renal function. The tetracyclines can also aggravate renal insufficiency.

The adverse effects of the tetracyclines on the fetus, and on infants and children up to about eight years old include: changes in bones and in the enamel and dentine of the teeth; discoloration of the teeth varying from gray to yellowish-brown to black; a transient inhibition of bone growth; hypoplasia of the tooth enamel and dentine; and discoloration of the nails and onycholysis following exposure to the sun. (Similar nail changes can also occur in adults.) Obviously, the tetracyclines should be prescribed during pregnancy and early childhood only if a less toxic drug is unlikely to be effective. Photosensitivity reactions have been reported with all tetracyclines, but they occur most frequently with the longer-acting tetracyclines, demeclocycline, methacycline, and doxycycline.

Reprinted from *The Medical Letter on Drugs and Therapeutics*, New York, N.Y. Vol. 11, no. 15, July 25, 1969.

MEETINGS

GENERAL

September 24 5:00 P.M.
177th Semi-Annual Meeting of the Hartford County Medical Association
Hartford Hilton, Hotel, Hartford
Speaker: Victor R. Fuchs, Vice President in Charge of Research, National Bureau of Economic Research. Subject, "The Economists Rx for the Medical Care Industry."

October 1
177th Semi-Annual Meeting of the Fairfield County Medical Association
Greenwich Country Club
October 23
186th Semi-Annual Meeting, New Haven County Medical Association
Waverly Inn, Cheshire
Business Meeting 3:00 P.M.; Social Hour and Dinner to follow

MEDICINE

Tuesday 5:30 P.M.
September 9-June 16
Immunology and Immunologic Diseases and Clinical Pharmacology
Lawrence and Memorial Hospitals Auditorium, New London
Eighth series of courses (20) in basic sciences as related to clinical medicine. Participants completing the course will be granted 40 hours of postgraduate credit by the Connecticut Academy of General Practice. Registration limit, 75; fee \$115 for the 20 seminars. Course Director, Edward Gipstein, M.D., Director of Medical Education and Chief, Department of Medicine, Lawrence and Memorial Hospitals; co-director, Richard Gorlin, M.D., Associate Professor of Medicine, Harvard Medical School, and Chief, Cardiovascular Division, Peter Bent Brigham Hospital.

September 25 8:30 A.M.-5:00 P.M.
18th Annual Scientific Symposium, Connecticut Academy of General Practice
Hartford Hilton Hotel, Hartford
Morning session, Lectures on "Atypical Chest Pain," "Differential Diagnosis of Abdominal Pain," "Diagnostic and Therapeutic Uses of Electronic Instruments." Afternoon session, panel on "Drug and Their Relation to Sex and Rebellion." Luncheon speaker, reception, program for the women. Additional information write or call the Academy Executive Office, 179 Allyn

Street, Hartford; phone 246-6566.
Regional Meeting (New England, Canada) of the American College of Physicians
Mary S. Harkness Auditorium, Yale Medical School
October 10 8:30 A.M.-5:30 P.M.
Peter Bent Brigham Postgraduate Medical Series
"Diseases of the Adrenal Cortex: Diagnosis and Management"
George W. Thorn, M.D., Hersey Professor of Medicine, Peter Bent Brigham Hospital
Fee, \$300 per course; contact David P. Lauer, M.D., Peter Bent Brigham Hospital, Boston, Mass.

PEDIATRICS

November 19
Annual Pediatric Symposium
St. Francis Hospital, Hartford
"Principles of Immunology and Infectious Diseases Applied to the Care of Children"
All participants are members of the faculty of the Albert Einstein College of Medicine.
For additional information contact William E Hart, Director of Pediatrics, St. Francis Hospital Hartford.

SURGERY

October 1 1:30 P.M.
Fourth Annual Combined Clinical Meeting of Section on Ophthalmology, Connecticut State Medical Society, and Yale Medical School.
1:30 P.M. Yale-New Haven Medical Center Eye Clinic for examination of cases; 3:00 P.M., discussion of cases, Brady Auditorium; 4:00 P.M., business meeting, CSMS Eye Section, Brady Auditorium; 6:00 P.M., Social Hour, Park Plaza Hotel; 7:00 to 9:00 P.M., Dinner, Park Plaza Hotel, Guest Speaker, Lorenz E. Zimmerman, M.D., Director of Ophthalmic Research, Armed Forces Institute of Pathology, Walter Reed Medical Center, Washington, D.C., topic, "Pathological Consideration in the Management of Tumors of the Iris and Ciliary Body."
Program chairman, Dewey Katz, M.D., CSMS Eye Section, assisted by Daniel M. Albert, M.D., Assistant Professor of Ophthalmology, Yale Medical School
January 15, 1970
Conference, Connecticut Chapter of the American College of Surgeons
Park Plaza Hotel, New Haven
Contact: Francis M. Hall, M.D., 140 Woodland Street, Hartford

Connecticut Medicine

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editorials

Smoking Habit Among Teen-agers

The relation between cigarette smoking and many serious diseases of the lungs and vascular system has been generally accepted since the Surgeon General's report in 1964 and frequently referred to in these pages. The report also drew attention to the lack of information on the psychosocial aspects of smoking and urged that more research be undertaken on this aspect. Thomas¹ analyzed smoking habits and thoughts about smoking by New Haven County physicians and Yale Medical faculty in December of 1968.¹ Boyle's paper² now presents some findings of a questionnaire survey designed to determine the smoking habits and attitudes of teen-age school children and assess the factors involved in starting and stopping the smoking habit.

The questionnaire was specifically designed for such a study and contained separate sections for present smokers, former smokers, and non-smokers, as well as a general section for all subjects to answer. The pupils were mostly sixteen to seventeen years of age. The response rate was 80 per cent and the total sample were found to have interpreted and answered the questions correctly. There have already been a number of studies on the smoking habits of British school children, but the results have varied widely to some extent owing to differences in definitions of present and former smokers and non-smokers as well as purely regional differences in smoking habits. In Boyle's survey of Glasgow the prevalence of smoking in girls was less than boys as was also found in the results elsewhere in this issue. The number in Boyle's study are small compared to the study reported in this issue. The population studied was relatively select also. However the results are a pointer to further research in this group.

In Bothwell's study of rural school children 15.3 per cent of present smokers and 84.7 per cent of non-smokers were aware of the connection between cigarette smoking and lung cancer. In Boyle's study the pupils are better informed. Nevertheless 76 per cent of the present smokers continued to smoke despite their knowledge of the relation. Health education clearly needs to focus attention to the connection between smoking and cancer, bronchitis,

coronary heart disease and high blood pressure in a way that knowledge of the relation will deter the pupils from smoking. It seems probable that these consequences which must seem remote to school children are not in fact good education points and that other factors of more immediate concern to them such as impairment of athletic performance, increased danger of accident on the highway, by carbon monoxide in tobacco smoke increasing reaction time, should be given more prominence.

Other studies have also showed an inverse relation between smoking and academic achievement. This fact might well be used with advantage in anti-smoking propaganda directed to this age group, although it cannot of course be claimed that stopping smoking would lead to increased academic ability. The number of cigarettes smoked per day by the different groups showed that among smokers the percentage of boys smoking more than five cigarettes per day was about twice that of girls. Among former smokers, however, the percentage smoking over five cigarettes per day was about the same for boys and girls. This means that proportionately more girls stopped smoking than did boys.

Pupils who started smoking to help nervousness were less likely to have stopped smoking than those who started for other reasons. Such a finding could be emphasized in anti-smoking propaganda to underline the essentially drug-like nature of the smoking habit. Study of the factors involved in stopping smoking shows that of those who tried to stop smoking because of the expense incurred, only 41 per cent succeeded, whereas 83 per cent of those who tried to stop for other reasons were successful.

These results suggest that increasing the cost of cigarettes might not be a good way to reduce the number of teen-agers who smoke. Furthermore, a gradual reduction in cigarette consumption is not an effective way to stop smoking. The patient who says he "will try" rarely carries through. The patient who says "I will" often succeeds.

L.H.N.

References

1. Thomas, N.: Smoking attitudes of New Haven County physicians. *Conn. Med.*, 32: 902, December 1968.
2. Boyle, C. M.: Some factors affecting the smoking habits of a group of teenagers. *Lancet*, II: 1287, December 14, 1968.

Curing Osteoporosis With Thyrocalcitonin

Osteoporotic bone loss is a health problem of major magnitude and might be considered the worlds most common illness. It is not just the problem of fragile, inactive elderly people. It is worldwide. Bone loss is a general phenomenon beginning by the fifth decade in both sexes but progressing more than twice as fast in the female as in the male. Among contemporary American women there are 4.5 million who suffer from hip fractures, vertebral decalcifications and even collapse of some vertebra. Then there is the serious alveolar bone loss which leads to diminution of tooth support, fenestration of the roots and actual loss of teeth.¹

Calcium intake does not seem to relate to bone loss. Intake of as much as 1500 mg. calcium per day does not seem to protect against osteoporosis and levels of intake as low as 300 mg. per day do not seem to contribute to osteoporosis. Most patients actually take in enough calcium in the diet to maintain an appropriate calcium balance and yet there is an irreversible daily loss of 30 mg. of bone calcium after age 40. The skeleton is inevitably losing 900 mg. calcium a month, 9 grams a year and 450 grams over a five decade period. What then is the best protection at present against inevitable decalcification of bone.

In the past it has been fairly well documented that deficiencies in anabolic hormones particularly androgens, estrogens, and possibly growth hormone may be operative. We know that there is regression of bone mass which parallels the equally universal decline in hormones which retard bone resorption. The prevalence of adult bone loss may be and seemingly is inexorable except in those regions where the fluoride content of drinking water is high. The question, however, remains whether we must accept bone loss as inevitable.

Parathormone tends to draw calcium out of bone whereas thyrocalcitonin antagonizes this action.² This latter hormone therefore should be of use in the maintenance of the skeleton and could be therapeutically valuable in various types of osteoporosis, Paget's disease, hyperthyroidism, that due to chronically bed-ridden patients and paradentosis. In these columns it was predicted² that when thyrocalcitonin becomes available for clinical trial it could very well serve to assist in the stabilization of bone and the prevention of osteoporosis. There are now two Swiss pharmaceutical companies, Ciba and Sandoz

and Lederle Lab in this country that have synthesized pig thyrocalcitonin.

Dr. Gerard Milhaud of Hospital Saint-Antoine Paris has just reported to the French Academy of Sciences of his results with the use of thyrocalcitonin upon three female patients age 57, 67 and 69, with severe osteoporosis who had been bed-ridden, in spinal casts to ease their pain and lessen the dangers of bone fractures.³ He injected them three times a week with 5 micrograms of thyrocalcitonin that had been extracted from pig thyroid in his laboratory. After four months of treatment with the hormone, the pain disappeared and now the patients are able to walk normally.

Tracer tests with radioactive calcium showed a marked shift from calcium negative to a positive calcium metabolism in all three patients. One patient who had been losing 356 mg. calcium a day showed a daily gain of 298 mg. Dr. Milhaud is currently comparing the efficacy of thyrocalcitonin extracted from various animals including pigs, salmon and a human being. The human hormone was extracted from a rare case of medullary thyroid cancer that produced 1,000 times the normal amount and measurements of its level in blood is used as an accurate warning signal for that type of cancer.

With the striking success of curing osteoporosis with thyrocalcitonin, it is hoped Milhaud and others will now go on to speed the mending of bone fractures to arrest paradentosis and Paget's disease. Perhaps the time will come when thyrocalcitonin will be given preventively to stave off the onset of osteoporosis. We are at the threshold of the conquest of the "worlds most common illness."

L.H.N.

References

1. Nahm, L. H.: Nutrition and osteoporosis. *Conn. Med.*, 32: 336, May 1968.
2. Nahm, L. H.: An approach to the treatment of osteoporosis. *Conn. Med.*, 32: 492, July 1968.
3. Thyrocalcitonin restores bones. *Scientific Research*, 4: 15, 1969.

An Experiment In Penal Reform

Nature¹ states that more than half of the British prison population of 1961 had been in prison before. Britain now spends some 30 million pounds a year on prison service, an average weekly cost of 14 pounds per prisoner. If more than half the people who have received this expensive treatment can be expected to commit further crimes on their release, it is hard to be satisfied that prison either



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benefits the prisoner or protects society. The figures for this country are equally dismal.

Since 1948 it has been judicial policy in Britain to send increasingly fewer categories of offenders to prison. It is the first glimmerings of experiments in penal reform. Other countries have been much freer to conduct experiments in penal reform which may bring envy to western penologists. For example Zanzibar is to abolish courts of law and prison sentences for all crimes other than murder and robbery with violence.

The governing council of the island hopes to eliminate prisons altogether and in the future offenders will be sent to penal reform institutions for five years where they will be taught a trade and rehabilitated. The Zanzanian High Commission in London has not yet received details of these reforms so it is hard to assess their significance. For example it is not known what rights of defense will be accorded those accused of crimes, and although it may be a fine ideal to abolish prisons, "penal reform institutions" could be different in name only. Nevertheless Zanzibar has built into its experiment in penal reform the ideal of "treatment not punishment."²

Announcing the reform, the President of Zanzibar said that poverty was the principal determinant of crime and that the government would concentrate on raising the standard of living. Undoubtedly poverty is related to crime and in Zanzibar this may be the major determinant, but in this country there is also drug addicts, alcohol victims and psychiatric irrationality also which plays a role in crime besides poverty. The Zanzibaris may be naive in supposing that increased wealth will diminish crime or that offenders will be reformed by the acquisition of an honest trade. Nevertheless, there is much to be gained from experimenting with the conventional penal system. We all know that prisons are expensive, degrading and lamentably inefficient in performing their stated aims. No more devastating indictment of this system can be found anywhere than Koskoff and Goldhurst's description of the life history of a criminal in "The Dark Side of the House."³

The Zanzibaris are about to carry to a logical conclusion the British policy of sending fewer categories of offenders to prison. The results of this experiment, and we hope it has been properly set up, will be watched with great interest, and if successful with envy by western penologists.

L.H.N.

References

1. No prisons for Zanzibar. *Nature*, 219: 430, August 3, 1968.
2. Nahum, L. H.: Cooperation between law and psychiatry. *Treatment—not punishment*. *Conn. Med.*, 31: 240, April 1967.
3. Koskoff, Yale D. and Goldhurst, Richard: *The dark side of the house*. Dial Press, 1969.

The Health Center Movement: I.

The health center movement began in the early 1900's to help solve health problems of the poor. Undernutrition and infectious diseases were prevalent in the slums and rational preventive measures of infant feeding and immunization were at hand. Some of the reformers behind the movement also expected that the centers might also become an institution for the reform of medical practice outside the hospital, for the renewal of community life and even for the rehabilitation of the poor out of the state of poverty itself. It is therefore not surprising that in real life both public and private action were confined only to districts full of poor people. The health center supporters showed the same political, ethical and religious rationale of the Progressive Era aimed at the uplift of the poor.

A stage in the development of this idea was devised by Phelps¹ who enlisted neighborhood residents as "aides" to recruit patients, to take household surveys and to participate in governing of the centers. From each neighborhood block a resident was selected to be a personal contact for all the mothers, bringing them to the center. By this means 100 per cent participation was achieved. Some neighborhood aides also helped in taking a home census. Neighborhood residents chosen on the basis of the block in which they lived and advisors from the district chosen on the basis of their occupations were to be on the board of management of the health center. The outcome was to be two-fold: a greater sense of community and maximum use of health services. The democratic ideal of citizen participation in civic life was also to be a motivating force for health action.

Such a plan met much resistance from many forces and lacked political support of the municipal government and aroused public suspicion that the social unit might in fact really be socialistic if not communistic.² Others, however, judged the features of health centers to be the results more of indifference in the neighborhoods rather than of hostile political interference. They were individualistic about health but socialistic about education.

In rural health centers, the idea was to provide costly modern workshops for doctors who were not

nationally inclined to take up practice away from the city or to enter into group practice by themselves.³ To increase the clinical span and the output of scarce medical personnel, the use of paramedical people such as nurses and technicians was undertaken. In a few curative centers, the coordination was of clinical practice in groups or teamwork to solve the central treatment problem of personal and integrated care of the patient, more a response to medical specialization.

Pomeroy's "curative" health centers in California were essentially local outpatient clinics and coordinated the work of doctors, nurses and social workers in their dealings with a wide range of problems for which people sought medical help. Their scope was treatment rather than the traditional public health practice of infant feeding, the follow-up and screening and treatment of venereal disease. The health center enthusiasts viewed the programs of centers as preventive and educational complementing the curative work of private practice and carefully avoiding competition with it. In the United States private practice was dominant except for treatment of tuberculosis and venereal diseases which were relegated to public agencies.

In other countries especially in rural regions, the health centers seldom made distinctions between treatment and prevention. The preventive problems were derived from community problems which were infectious diseases and poor nutrition. Immunizations, vaccination, infant feeding, the screening for and treatment of venereal diseases were the major techniques. Similarly the centers operation was to be responsive to community experience as a result of district locations and community participation. The programs of some centers, however, went far beyond medical and welfare activities to include recreation, day care for children and clubs. Such programs implied a view of health as a way of living not just freedom from disease. However, not every one saw the programs of health centers as deriving from local community needs and expectations or from a social view of health.

The health center implied a relation to other situations and it was the "other" namely the hospital that determined the centers function and program. For the center was in a certain district with a given population and it served as a means for triage of patients for the hospital. Illness could be sorted out by its clinical severity and allocated to the hospital according to the needs for technical treatment that was available in the hospital. The center would thus deal with what illness that did

not get referred. Its functions derived from the internal needs of the hospital and were often viewed as leftovers, chronic illness and disability.

The British plan for health centers was an example of planning implicitly based on the primacy of hospitals and separate districts of population.⁴ The separated duties of the doctor, midwife and nurse were to be administratively joined together in a health center. Like general practitioners, the centers would be linked to hospitals by referrals. Coming shortly after World War I, the plan was somewhat like that in the military medical service where the wounded were sorted out according to severity and allocated for front aid stations or the rear (hospitals).

As a hospital outpost or first aid station the health center would treat only simple not complex illnesses even though in actual fact prevention and chronic illness in the community were exceedingly complex and are still even more so today. Perceived as hospital outposts dealing with supposedly simple community health problems, centers everywhere often had exceedingly great difficulty in attracting professional staff and maintaining any kind of programs of their own.

The health center movement also developed in many other places throughout the world. Centers became a part of government systems of health care in such countries as Russia, Chile and Yugoslavia. The English plans, however, were never realized. Grant⁵ was interested in centers for rural community development first in China and later in Puerto Rico and a community health center was begun by Kark in South Africa⁶ the so-called Pholela health center. In this country, however, the health center movement declined in the late 1930's but it is reappearing today.

L.H.N.

References

1. Phillips, W. C.: *Adventuring for democracy*. New York Social Unit Press, 1940, p. 46.
2. Stoeckle, J. D. and Candib, L. M.: *The neighborhood health center—Reform ideas of yesterday and today*. *New Eng. J. Med.*, 280: 1385, June 19, 1969.
3. Mountin, J. W. and Hoenack, A.: *Health center: adaptation of physical plants to service concept*. *Pub. Health Rep.*, 61: 1369, 1946.
4. Great Britain, Consultative Council on Medical and Allied Services. *Intern. Report on the Future Provision of Medical and Allied Services*, London. His Majesty's Stationery Office, 1920.
5. *Health Care for the Community: Selected Papers*. Edited by C. Seipp, Baltimore. Johns Hopkins Press, 1963. (No. 21 American Journal Monograph Series).
6. Kark, S. L. and Cassel, J.: *Pholela Health Center: Progress Report*. *South African Medical Jr.*, 26: 101: 4, 132, 1952.

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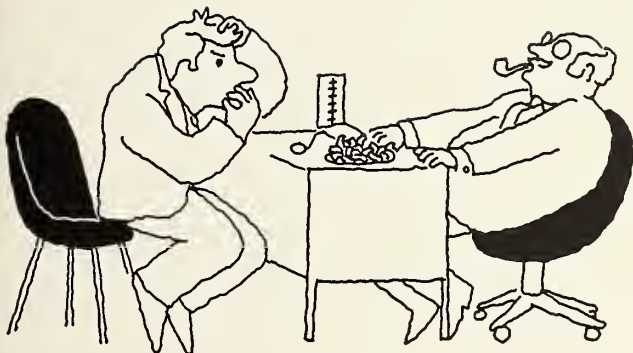
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Avoiding Potassium Loss From Thiazide Therapy

Thirty to forty per cent of hypertensives treated with thiazides have a lowering of potassium levels to below 3.5 mEq./liter. This same may be said for patients with cardiac failure who are treated with digitalis as well as with thiazides. Since lowering of serum potassium levels renders the heart more susceptible to abnormal rhythms during digitalis therapy, two important questions present themselves. One is whether the body is able to adjust to initial potassium loss by some sparing mechanism which would protect the body against depletion of potassium reserves. If there is no sparing mechanism and there occurs a steady uninterrupted loss of potassium reserves, what therapeutic measure is available to us to protect the patient against hypopotassemia.

In the case of sodium we know that there is a sparing mechanism. In the first several days after diuretic therapy has been started, there is an initial sodium loss, but soon aldosterone is secreted, sodium is spared and no depletion of body sodium takes place thereafter. If this is the mechanism of sodium sparing one should expect continued potassium depletion since aldosterone facilitates potassium loss as it preserves sodium. There is, however, some question as to whether long term therapy with thiazides do reduce potassium stores. "Exchangeable" potassium determinations have been reported as showing no significant potassium loss.¹

Maronde and his associates² have addressed themselves to the solution of this problem by studying eight men with mild to moderate uncomplicated hypertension who had normal renal function. They found after a control period that a dose of 150 mg. hydrochlorothiazide daily resulted in a loss of sodium during the first three days of therapy followed by a period of sodium retention from the fourth to eighth day of treatment. At the same time potassium loss was also marked during the first three days of thiazide administration, but in contrast to sodium there developed no subsequent potassium retention. Instead the serum potassium dropped steadily from an average control level of 4.1 down to 3.2 mEq. per liter by the end of the first week of therapy and remained near this level. The clue to this difference came from their aldosterone excretion rates which rose from an average control level of 10.7 up to 20.8 micrograms per day. This increased level of aldosterone production continued throughout this study.

There was thus significant evidence for self-correction in the sodium loss, but no self-correction of potassium loss during thiazide therapy. The explanation for this seems to lie in the aldosterone excretion rate which was low in the normal range during the control period and increased with therapy, thus promoting sodium retention and continued potassium wastage.

What is additionally significant was that individual serum potassium levels were a poor index of the total potassium loss. The largest cumulative loss was found in those patients who had a serum level below 3.0 mEq. per liter. Increases in blood pH., pCO₂, and bicarbonate levels also correlated well with the potassium loss, but not with the state of sodium balance. If serum potassium levels can remain at a low normal range while tissue depletion of potassium consistently occurs, we may here find the explanation why hearts on digitalis may become irritable during thiazide therapy even before serum potassium levels reveal the deficiency.

If the body is constantly losing potassium during thiazide therapy via increased aldosterone secretion, it is clear why thiazide therapy should not be given alone but should be administered together with an aldosterone antagonist for example hydrochlorothiazide plus spironolactone (aldactazide) to avoid potassium depletion, cardiac arrhythmias and other undesirable consequences of this iatrogenic abnormality.

L.H.N.

References

1. Talso, P. J. and Caraballo, A. J.: Effects of benzothiadiazine on serum and total body electrolytes. *Ann. N. Y. Acad. Sc.*, 88: 822, 1960.
2. Maronde, R. F., Milgrom, M. and Dickey, J. M.: Potassium loss with thiazide therapy. *Am. Ht. J.*, 78: 16, July 1969.

Insulin And Atheroma

The importance of dietary fat has been stressed as an etiological factor in coronary artery disease (CAD). Recently, however, it has been observed that dietary sucrose correlates more closely with CAD. Yudkin¹ found that in young men on a high sucrose diet for 2 weeks, 6 developed hyperinsulinism together with an increase in weight of about 5 pounds, and also an increase in platelet adhesiveness. It is tempting to see here a link between sucrose ingestion, hyperinsulinism, overweight and a change in platelet behavior that could initiate atherosclerosis. None of these effects were seen in the other 13 men.

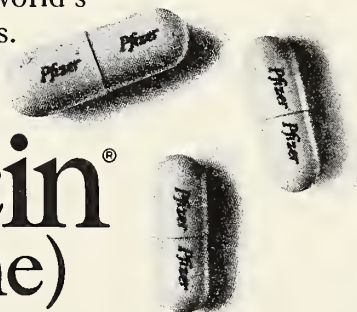
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Note: With oxytetracycline, phototoxicity is unknown and photoallergy very rare.

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All 19 showed an increase in triglyceride levels. The effects of sucrose were reversed almost entirely in 2 weeks when the subjects reverted to their normal diets. Szanto and Yudkin² have also shown that these effects can be reversed if subjects are given phenformin. They are also examining the effect of exercise, which is known to reduce insulin levels, upon the rise of insulin caused by sucrose in the susceptible persons. Thus sucrose can be added to the list of factors that induce hyperinsulinism, triglyceridemia and so promote atherogenesis. It should be noted that only a proportion of the population is susceptible to sucrose induced hyperinsulinism. These investigators have also reported a significant correlation between sugar intake and insulin levels and also platelet adhesiveness in a group of men with obvious occlusive atherosclerotic disease and no such correlation in a group of men selected for the absence of disease.

Stout and Vallance³ have found also that the majority of patients with CAD have elevated insulin responses to glucose with or without fasting insulin levels. Those abnormalities are present even in non-obese patients with myocardial infarction. South African Bantus who have an extremely low incidence of ischemic heart disease have an insulin response to an oral glucose load that is only 50 per cent of the response of white subjects to an identical stimulus. On the other hand physical exercise which is thought to retard or prevent atheroma formation results in carbohydrate utilization with reduced insulin requirements.

If elevated insulin response to carbohydrate is a factor in atherogenesis, by what mechanism can it do this? Probably it is through the metabolic mechanism of elevated serum triglycerides. Elevated serum triglycerides have been found after insulin shock treatment. Reduction of sugar intake and substitution of starch for sugar results in a fall in both triglycerides and insulin levels. Tolbutamide causes an elevation of insulin and triglyceride levels while phenformin decreases circulatory insulin, triglycerides and also cholesterol. And as noted above exercise which spares insulin also results in a fall in triglyceride and cholesterol levels. Finally in diabetes a potent cause of atherosclerosis there are increased triglycerides and often cholesterol.³

Of great interest are the reported correlations between glucose, insulin and lipids. In subjects with fasting normoglycemia, glucose and triglyceride levels are significantly correlated, but in hyperglycemia this relationship is lost. A recent study has shown that the blood sugar response to oral glucose

in non-diabetic man is related to fasting plasma triglycerides and cholesterol and to the insulin response. It would appear probable that the primary cause of elevated triglycerides concentration are carbohydrate induced, and is directly related to the insulin response produced by that diet.³

Elevated insulin levels are probably factors in the well known association between obesity and CAD. Both in diabetic and non-diabetic subjects elevated serum cholesterol and triglyceride levels are found. It would appear that body weight and the insulin response to glucose are interrelated and act together to correlate with triglyceride. In view of the well known properties of insulin in stimulating lipogenesis and inhibiting lipolysis, it is tempting to believe that hyperinsulinism here also is the primary disorder.

High insulin levels have been found in patients with hypertension which is an important factor in ischemic heart disease. Yudkin¹ points out that smoking could well be added to the list of factors that link atherogenesis with insulin since smoking which is epidemiologically associated with ischemic heart disease also has been shown to induce hyperinsulinism. So far the evidence which links hyperinsulinism to atherogenesis is strong. The question remains why in diabetes where there is impaired insulin production we also have high incidence of atherosclerosis.^{4,5,6} Does diabetes operate through a different mechanism or is it possible to find a common denominator.

Diabetes mellitus is characterized by a relative deficiency rather than an excess of circulating insulin. Both in juvenile and maturity onset diabetes there is a reduced insulin response to glycemic stimuli when compared with controls of similar body weight. All types of diabetes have a delayed sluggish and reduced insulin response to a glucose infusion.² From this knowledge and others it is becoming clear that the feature common to all stages in the diabetic syndrome is a decreased insulin response to hyperglycemia. However, hypertriglyceridemia is a universal finding in diabetes mellitus and has also been found in patients with a strong family history of diabetes after carbohydrate ingestion. Perhaps the common link between insulin induced atherosclerosis and diabetes is elevated serum lipids and triglycerides.

There is another possibility namely that there exists antagonism to the action of insulin in some patients with high insulin levels. If patients with high insulin levels have insulin antagonism in the form of synalbumin³ or growth hormone or steroid

excess, then there might be a deficient net insulin activity as a possible link between the two groups. In either case what is common in the two groups is hypertriglyceridemia and hyperlipemia.

L.H.N.

References

1. Yudkin, J.: Carbohydrate metabolism and its disorders. Edited by F. Dickens, P. J. Randle and W. J. Whelan, p. 169. London, 1968.
2. Szanto, S. and Yudkin, J.: Letter to the editor in *Lancet*, I: 1211, June 14, 1969.
3. Stout, R. W. and Vallance, Owen J.: Insulin and atheroma. *Lancet*, I: 1078, May 31, 1969.
4. Warren, S., LeCompte, P. M. and Legg, M. A.: The pathology of diabetes mellitus. London, 1966.
5. Mahler, R. F.: Diabetes mellitus. Edited by L. J. P. Duncan. Edinburgh, 1966.

Phenformin And Ethylestrinol In Venous And Arterial Thrombosis

For years now anticoagulants have been prescribed for patients during and after arterial occlusions, particularly myocardial infarction. In the latter instance the rationale has been to prevent venous thrombosis and resulting pulmonary embolism, to reduce the admittedly infrequent intramural thrombosis and peripheral embolization. In the post-infarction period the reasoning has been to prevent recurrence of arterial occlusion.

We now know that the venous thrombus is different structurally than is the arterial thrombus and that treatment or prophylaxis of the former requires different modalities than treatment of the latter. The venous or red thrombus is composed of a solid mass of red cells, fibrin and plasminogen. The arterial or white thrombus consists primarily of a mass of platelets stuck together and adherent to collagen exposed when the endothelium over an atheroma disappears.

Deep vein thrombosis results from the interaction of two factors, reduced velocity of blood flow and hypercoagulability. Early ambulation, exercises and elastic stockings have come into use to eliminate the factor of sluggish circulation in the extremities. However, when deep vein thrombosis is not prevented by such measures, it can be influenced by anticoagulant drugs and fibrinolytic therapy. The routine post-operative use of anticoagulants, however, can hardly be a practical proposition. Accordingly once a thrombus has formed fibrinolytic drugs seem to be the best prospect.

The theoretical basis for this treatment is that plasminogen is present in every red thrombus and

its activation to plasmin by an activator either streptokinase or urokinase will cause digestion of fibrin in the clot to form soluble polypeptide fragments. There is, however, a time element involved which is important. After 48 hours the thrombus will begin to organize and then plasmin will have little chance to dissolve the clot.

Urokinase is a good activator of the fibrinolytic system because it is a normal constituent of human urine and it is free of the antigenic properties of agents such as streptokinase. Unfortunately it is not commercially available and therefore most trials of fibrinolytic therapy have been made with streptokinase. This latter, however, has to be given by continuous intravenous infusion for a period of 7-10 days. In patients in whom it has been tried, it does lead to rapid disappearance of tenderness often within 12 hours and complete clearance of thrombus in over half of the patients. Most patients, however, develop pyrexia and some develop bleeding.¹

Comparing this group with heparin, 6 out of 10 showed complete dissolution of thrombus with streptokinase while only 2 out of 10 showed complete dissolution with heparin. If one can achieve early dissolution of thrombus with any method it will prevent permanent vein damage. While streptokinase seems to be effective in dispersing red thrombi, its use is certainly not without hazard and its value in reducing mortality of deep-vein thrombosis is yet to be established. Since the fibrin deposition mechanism is not involved in platelet thrombus formation, success in dispersing a platelet thrombus is not yet in sight and it is doubtful that a purely fibrinolytic agent such as urokinase or streptokinase will furnish the answer to prevention of arterial occlusion.

A substance which could act to increase fibrinolytic activity but that also reduces platelet stickiness might be the answer to both venous and arterial thrombosis. Fearnley now reports in *Lancet*² a combination of phenformin and ethylestrinol which promises to accomplish just this. In 1967 he and his co-workers gave phenformin 50 mg. bid and 4 mg. ethylestrinol bid by mouth to humans and found that this combination produces sustained increase in blood fibrinolytic activity as judged by reduction in both the dilute blood-clot and euglobulin-lysis time, reduces plasma fibrinogen and serum cholesterol levels in arteriopathic patients. Furthermore, this combination of drugs also reduces platelet stickiness in glass in over three-quarters of the patients and is maintained with continued treatment.

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INDICATIONS: Patients with moderate to severe anxiety and/or agitation and depressed mood; patients with depression in whom anxiety and/or agitation are severe; patients with depression and anxiety in association with chronic physical disease; schizophrenics with associated depressive symptoms.

CONTRAINDICATIONS: Central nervous system depression from drugs (barbiturates, alcohol, narcotics, analgesics, antihistamines); bone marrow depression; urinary retention; pregnancy; glaucoma. Do not give in combination with MAOI drugs because of possible potentiation that may even cause death. Allow at least 2 weeks between therapies. In such patients therapy with TRIAVIL should be initiated cautiously, with gradual increase in the dosage required to obtain a satisfactory response.

WARNINGS: Patients should be warned against driving a car or operating machinery or apparatus requiring alert attention, and that response to alcohol may be potentiated.

PRECAUTIONS: Suicide is always a possibility in mental depression and may remain until significant remission occurs. Supervise patients closely in case they may require hospitalization or concomitant electroshock therapy. Untoward reactions have been reported after the combined use of antidepressant agents having various modes of activity. Accordingly, consider possibility of potentiation in combined use of antidepressants. Not recommended for use in children. Mania or hypomania may be precipitated in manic-depressives (perphenazine in TRIAVIL seems to reduce likelihood of this effect). If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Caution patients about errors of judgment due to change in mood.

SIDE EFFECTS: Similar to those reported with either constituent alone.

Perphenazine: Should not be used indiscriminately. Use caution in patients with history of convulsive disorders or

severe reactions to other phenothiazines. Likelihood of untoward actions greater with high doses. Closely supervise with any dosage. Side effects may be any of those reported with phenothiazine drugs: blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); extrapyramidal symptoms (opisthotonos, oculogyric crisis, hyperreflexia, dystonia, akathisia, dyskinesia, parkinsonism) usually controlled by the concomitant use of effective antiparkinsonian drugs and/or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine; severe acute hypotension (of particular concern in patients with mitral insufficiency or pheochromocytoma); skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; endocrine disturbances (lactation, galactorrhea, disturbances of menstrual cycle); grand mal convulsions; cerebral edema; altered cerebrospinal fluid proteins; polyphagia; paradoxical excitement; photophobia; skin pigmentation; failure of ejaculation; EKG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonic-like states; autonomic reactions such as dryness of the mouth, headache, nausea, vomiting, constipation, obstipation, urinary frequency, blurred vision, nasal congestion, and a change in the pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude; muscle weakness; mild insomnia; significant unexplained rise in body temperature may suggest intolerance to perphenazine, in which case discontinue. Antiemetic effect may obscure signs of toxicity due to overdosage of other drugs or make diagnosis of other disorders such as brain tumors or intestinal obstruction difficult. May potentiate central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol), atropine, heat, and phosphorous insecticides.

Amitriptyline: Careful observation of all patients recommended. Side effects include drowsiness (may occur within the first few days of therapy); dizziness; nausea; excitement; hypotension; fainting; fine tremor; jitteriness; weakness; headache; heartburn; anorexia; increased perspiration; incoordination; allergic-type reactions manifested by skin rash, swelling of face and tongue, itching; numbness and tingling of limbs, including peripheral neuropathy; activation of latent schizophrenia (however, the perphenazine content may prevent this reaction in some cases); epileptiform seizures in chronic schizophrenics; temporary confusion, disturbed concentration, or transient visual hallucinations on high doses; evidence of anticholinergic activity, such as tachycardia, dryness of mouth, blurring of vision, urinary retention, constipation, paralytic ileus; agranulocytosis; jaundice. The antidepressant activity may be evident within 3 or 4 days or may take as long as 30 days to develop adequately, and lack of response sometimes occurs. Response to medication will vary according to severity as well as type of depression present. Elderly patients and adolescents can often be managed on lower dosage levels.

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Fearnley, as have others, believes that deposition and removal of fibrin is in continuous flux and that coagulation and fibrinolysis are in a state of dynamic equilibrium. This concept suggests that coagulation and fibrinolysis together form a whole, a physiological system of repair which uses fibrin as a cement and that imbalance of either side of the system leading to increment and persistence of fibrin especially on the walls of arteries could lead to arterial disease and other conditions.

The behavior of fibrinogen/fibrin may also be of importance in conditions other than occlusive vascular disease such as rheumatoid arthritis, cancer and nephritis. Accordingly, Fearnley's findings lend weight to the suggestion that the combination of phenformin and ethylestrinol merits treatment as a prophylactic measure in acute arterial and venous occlusions, after vascular surgery and insertion of cardiac prostheses. By increasing fibrinolytic activity, lowering serum cholesterol and reducing platelet stickiness it would seem these drugs have a wide spectrum of therapeutic possibilities in sufferers from vascular disease. They may also have application not only as a therapeutic agent but also as a research tool.

L.H.N.

References

1. Fibrinolysis and deep vein thrombosis. *Lancet*, I: 931, May 3, 1969.
2. Fearnley, G. R., Chakrabarti, R. and Evans, J. F.: Fibrinolytic and defibrinating effect of phenformin plus ethylestrinol in vivo. *Lancet*, I: 910, 1969.

The Hyperbetalipoproteinemias

There are at least three factors interacting to finally produce atheroma. One is injury to intima of the artery such as occurs in infections, following absorption of toxic products such as carbon disulphide as occurs in viscose rayon workers and those poisons inhaled in cigarette smoke. Another is metabolic factors intrinsic in the arterial tissue itself which control respiration, lipogenesis and lipoprotein transformation. The third important factor is the concentration in the plasma of beta-lipoproteins.

Interest in the last arose from the fact that feeding dietary cholesterol to some experimental animals has been shown to cause atherosclerosis with histologic features similar to those in man. It is worthy of note that plasma lipids themselves can't do this because there is no essential free lipid in plasma. Furthermore, it is the beta-lipoproteins which closely correlate with atherosclerosis whereas

albumin complexed non-esterified free fatty acids seem to be unrelated to the atheromatous process. The evidence for this comes from a variety of sources. The low density plasma beta-lipoproteins occur in every case of the disease and can be isolated from atheroma in man. In low incidence groups such as dogs, rats and cats we find an average 50 mg. per 100 ml. In man the average is 500 mg. per 100 ml.

In man the concentration of beta-lipoproteins may vary widely. At birth infants have 100 mg. per ml. In adults suffering from certain lipid transport disorders the figure may rise to 1,000 mg. per 100 ml. In malnourished individuals subsisting on a low diet in fat and deficient in proteins and calories, the beta-lipoproteins may be in the range 200-300 mg. per 100 ml. Alpha-lipoprotein complexes remain very constant in human subjects over this rather large variation in beta-lipoproteins. The incidence of atherosclerosis is very high in essential hypercholesterolemia and low in malnourished populations. In man with serum cholesterol and serum beta-lipoproteins in the normal range the correlation between concentration and disease is poor. Discovering individuals with high beta-lipoproteins in plasma could offer an important starting point for the control of atherosclerosis if we had methods to overcome this abnormality.

Levy and Fredrickson¹ have recently screened 5,000 plasma samples by the method of electrophoresis. They found 450 patients with familial hyperlipoproteinemia and suggest methods of therapy depending upon the specific type. In type I exogenous hyperlipemia there were only 50 documented cases. The plasma remains turbid 15 hours after the last meal and the turbidity is due to excess chylomicrons. This results from a severe deficiency in post-heparin lipolytic activity, the absence of an enzyme released by heparin which normally breaks the chylomicrons down to smaller particles. Such patients are already symptomatic before age 10. Their plasma triglycerides rise in patients on a regular diet and xanthoma develop. A low fat diet results in marked clearing of hypertriglyceridemia and disappearance of secondary manifestations of this disorder. Medium chain triglycerides (MCT) make an ideal dietary supplement, can be made quite palatable. Because they are transferred from the gastrointestinal tract directly to the blood instead of to chyle they do not affect the level of chylomicrons.

Over 50 per cent of the 450 were of type II. These are secondary to thyroid, renal or liver disorders

and may result merely when there is excess dietary cholesterol and saturated fats in the diet. In this group neither weight reduction nor exercise changes the lipoprotein pattern. It is the most serious of the hyperlipoproteinemias and often associated with advanced atheroma. Frequently they will exhibit premature coronary disease in the 3rd to 5th decades. They may have tuberous xanthoma, xanthelasma and circum cornei or merely premature coronary artery disease. They can be recognized from excess plasma cholesterol and beta-lipoproteins. Treatment requires reduction of cholesterol in the diet, prevention of its absorption from the gastrointestinal tract by cholestyramine or beta-sitosterol, increasing its metabolism by dextro thyroxin and use of clofibrate 500 mg. three or four times a day. Family screening will often uncover other patients.

Type III of beta-hyperlipoproteinemia consisted of 52 patients. The plasma is abnormally laden with triglycerides. There is also elevation of cholesterol. Arterial disease occurs with increasing incidence and severity in 4-5th decades. They may also have abnormal glucose tolerance as well as hyperuricemia. It appears that their plasma triglycerides are sensitive to both excess fat and carbohydrate in the diet. Such patients can be very responsive to specific therapeutic procedures. First is reduction to ideal body weight, maintenance on a low cholesterol and low carbohydrate diet and clofibrate. Even though such treatment seems to brighten the prognosis we are still not sure whether it will reduce or retard the associated atheroma.

Levy's type IV consisted of 99 patients. In this type cholesterol is normal. There is very high plasma triglyceride levels. In addition to atheroma they also exhibit retinitis, xanthoma, hepatosplenomegaly. The disorder probably represents an imbalance between synthesis and clearance of pro-beta-lipoproteins, at times due to overproduction or secondary to defect in clearance. Seventy per cent have diabetic oral glucose tolerance curve, 40 per cent have hyperuricemia. Obesity brings this disorder out in families. The treatment here is weight reduction to which the patients are universally responsive. With diet very low in carbohydrate, low cholesterol and high vegetables the pattern disappears when the ideal weight is reached. However, with dietary management and clofibrate they may respond much more effectively.

Levy's type V with 26 patients triglycerides may rise to 1,500 to 5,000 mg. per 100 ml. on a regular diet and there is also increased concentration of

cholesterol. It is generally secondary to a number of metabolic disorders including diabetic acidosis, alcoholism and pancreatitis. They have recurrent bouts of abdominal pain and occasional laparotomies are performed. There is an abnormal glucose tolerance and hyperuricemia. They are intolerant to ordinary dietary fats. However, even fat-free diets leave the triglyceride in range from 600-1,500. The recommended treatment is high protein, low fat and carbohydrate. Clofibrate may lower the triglycerides in some though not all. We still do not know the relation of this type to accelerated cardiovascular disease. The disorder is hereditary, because over half of the parents of these patients also exhibited type IV and type V lipoprotein patterns.

It is clear that to prevent further atherogenesis and arterial thrombosis, a program must be begun early and at any age in individuals with a family history. Beta-lipoproteins and triglycerides must be kept at as low levels as possible. The treatment must be long range because the illness takes from 10-20 years to produce complications. We must always remember that diet therapy aimed at weight control and beta-lipoprotein levels is intrinsically difficult to enforce because diet patterns are deeply rooted in culture and custom and are an integral part of psycho social behavior. We are fortunate to have drugs for diabetes, hyperuricemia and clofibrate for hyperlipoproteinemia which can facilitate our task. The patients must be made to recognize the effort is lifelong but the rewards are high.

L.H.N.

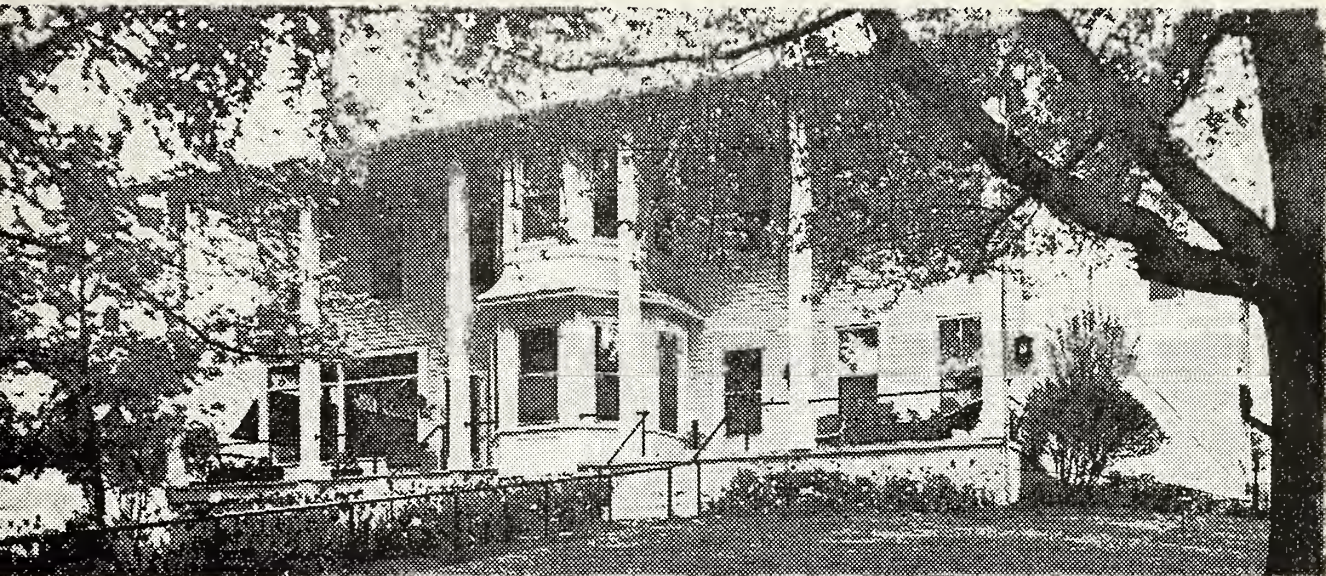
References

1. Levy, R. I. and Fredrickson, D. S.: Diagnosis and management of hyperlipoproteinemia. *Am. J. Cardiol.*, 22: 576, October 1968.

How To Gain The Value Of Ten New Medical Schools Without Building Them

Johnson and Hutchins¹ several years ago pointed out that of the 9,000 students admitted each year to medical schools about 10 per cent fail to graduate, this despite careful screening from more than twice the number of applicants. Ninety per cent of this attrition occurs in the first two years with more than two-thirds of it in the first year and most often it is the result of academic failure as measured by currently used examination techniques. In spite of this it is the rare student who fails because he lacks intellectual capacity to finish. This can be inferred from the fact that the medical school applicants have demonstrated the capacity to perform well in college have had very favorable recommendations

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and interviews and have had higher medical college admission test scores.

Physical disease is rarely responsible and there appears to be no evidence that it strikes more often in the first year than later. Strauss² points out that it is doubtful that the low attrition rate in the clinical years results from removal of the "unfit" earlier because this would imply that the characteristics leading to success during the first two years are substantially the same ones that are important to the clinical years and in the subsequent career of the physician. Can it be that it is the method of testing which is at fault? If this were so then as a result of our own faulty evaluation of students we are losing over 900 additional physicians annually, the potential output of at least 10 new medical schools costing a billion dollars to build and over a hundred million each year to operate.

Our present test methods used by faculties are likely to be primarily at the information recall level whether the examination is an essay type or some other. Processes such as the application of knowledge to concrete situations, analysis, synthesis, judgment, all so important to the physician are seldom required in the first or second year. This is readily understandable because to construct such examinations requires the assistance of test-measurement specialists to whom individual departments do not often turn for help.³ As a result cognitive processes higher than recall and comprehension did not predominate in Part I National Board Examinations as of 10 years ago although it probably has improved somewhat since then. In Part III, however, examination questions requiring sequential analysis of a patient's problem, the successive steps that a physician takes in establishing a diagnosis and beginning therapy after his initial data, have been obtained, have been constructed and are employed.

The correlation of scores achieved in such examinations at one school with grade-point averages from the usual methods of examination were negligible.⁴ Clearly the kind of examination given in the first two years of medical school do not evaluate the type of cognitive processes required of the physician. This means that the academic drop-out of the first two years could very well possess the required attributes of a physician. Such attributes embrace many other features than the cognitive processes. Thus of the students repeating a year because of academic failure, 85 per cent did graduate.¹ The failures then seem to be due to inadequate demonstration of mastery of an overwhelming

body of factual knowledge which when needed can readily be found in a book.

This raises the question whether all the facts now demanded to be committed to memory are really essential. Several years ago an editorial writer in *Lancet*⁵ estimated that the minimum body of facts common to all physicians successful in their own specialties could be acquired in six weeks. Strauss² has estimated that the core of basic sciences known in common by all medical school professors could be learned in 12-18 weeks. One wonders what scores even younger professors not too long removed from their medical school days would achieve in basic science examinations. If there is a core of factual information that must be committed to memory (as a language is today) the question arises whether all students should be required to learn this material at a set pace.

Fortunately a large scale reassessment is now under way in which each of the basic science and clinical departments of 100 participating medical schools will evaluate the appropriateness and relevance of the questions asked in Part I National Board Examinations.¹

Several questions suggest themselves. Should all students be required to learn the material at a set pace or should we not allow each student to take a qualifying examination whenever he feels competent to do so? If he fails we perhaps should allow him to repeat until he can demonstrate competence (within some limit). Another is why we should not permit students to take notebooks and texts into the examination if we intend to assess the higher cognitive processes. Is this not what the physician does throughout his life when faced with a situation with which he is not completely familiar. In fact such problem solving examinations involving the ability to locate and employ factual information have been used for years in some non-medical institutions.

There remain still other problems relating to medical school drop-outs. Why for example cannot every student seemingly motivated for medicine force himself through the first two years as 90 per cent do. Are there psychodynamic factors that rob the student of motivation, confidence, concentration. Are the medical school faculties responsible for the attrition through inappropriate criteria for assessment that defeats the student in his first two years. Clearly more relevant criteria for admission, retention and graduation from medical schools must be found. They can be worth one billion dollars,

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References

1. Johnson, D. G. and Hutchins, E. B.: Doctor or drop-out? Study of medical student attrition. *J. M. Educ.*, 41: 1097, 1966.
2. Strauss, M. B.: Doctor or drop-out? *New Eng. J. Med.*, 280: 1417, June 19, 1969.
3. Effect of Research Emphasis on Evaluation of Learning. Workbook of the Institute on Research and Medical Education. Colorado Springs, Colorado. Dec. 3-7, 1961.
4. McGuire, C.: Process approach to construction and analysis of medical examinations. *J. M. Educ.*, 38: 556, 1963.
5. Leading Article: Curtailing Curriculum. *Lancet*, 1: 133, 1966.
6. Charvat, S., McGuire, C. and Parsons, V.: A review of the nature and uses of examinations in medical education. Geneva World Health Organization, 1968. Public Health Paper, No. 36.

Biological Methods To Replace DDT

United States entomologists appear close to an important advance in man's age-old war against insects that devour his crops. The attack is not spearheaded by the chemical insecticides such as DDT but rather by an expanding arsenal of biological controls. These are massive deployment of bugs that are harmless to man but prey on crop-destroying pests. These are also methods to achieve large scale sterilization of adult insects to disrupt their reproductive cycle. Finally there is the use of synthetic copies of the natural scents secreted by pest species to lure insects to their destruction.

Such biological control methods are showing high promise in field tests and some Agriculture Department officials predict¹ that in certain parts of the country biological warfare coupled with limited use of chemicals will soon make possible the almost complete eradication of the cotton boll-weevil now probably the nation's costliest single pest.

One of the promising experiments with biological techniques is now going forward in the Coachella Valley of Southern California where farmers used to spray more than 4,600 cotton acres with chemicals to combat pink bollworm infestations. Now most mornings before dawn these summer days a yellow Agriculture Department plane sweeps above the valley floor spewing out thousands of sterilized male and female adult bollworm moths through a tube projecting from the cabin. Chilled immobile at about 38 degrees, the grey-winged insects cascade into the warmer air, then revive to mate with normal adults in the cotton fields below. The union frustrates the pairing of fertile moths and produces no eggs or destructive larvae. Avoidance of insecti-

cide spraying helps preserve insects that normally prey on cotton pests other than the pink bollworm.

Another progress report comes from a cabbage patch near Columbia, Missouri. There the cabbage-worm, which is destructive to a variety of vegetables including spinach and broccoli as well as cabbage, has been frustrated by the release of a tiny parasite wasp. The wasp injects its eggs into the cabbage-worm eggs on plant leaves. When the wasp grubs emerge, they devour the host eggs. Employing this and other biological techniques, Dr. Frank D. Parker, a government entomologist has eliminated over 99 per cent of the cabbageworm from the test-plot, and all insecticides as well.

Government entomologists are pushing confidently ahead. The lead actually came in 1888 when one Agriculture Department pioneer found a lady beetle in Australia that preys on a pest called the cottony-cushion scale then threatening to wipe out California citrus groves. After two years of beetle shipments from Australia the scale was brought under control. However, interest in biological methods waned following the spectacular success of DDT and the rapid proliferation of chemical insecticides in the post-war years. By 1955 interest in the biological approach began to revive and some notable victories followed. In recent years massive releases of sterilized male screwworm flies have reduced the population of the southern and western cattle pest. Annual savings to livestock producers from Florida to California are estimated at 120 million. And the Japanese beetle which once chewed on nearly 300 species of U. S. plants has largely succumbed to a dusting program that spread a disease that attacked the beetle.

One important center, the Federal Entomology Research Laboratory at Columbia, Missouri has just this year begun producing sufficient wasp eggs for experimental use against the cotton bollworm in Texas and the apple-boring coddling moth larva in Indiana. As biological warfare against pests increases, the long lasting chemical insecticides like DDT are on the way out.¹

And well they should be. A ground swell of opinion is building up against further pollution of this country's air and water with dangerous pesticides. They remain for years in the ground. They enter the chain of food production, they build up in the fatty tissues of animals and human beings with harmful consequences.² This year Michigan barred all use of DDT. The Arizona Pesticide Control Board faced with the problem of too much DDT in milk ordered a one year halt to commercial

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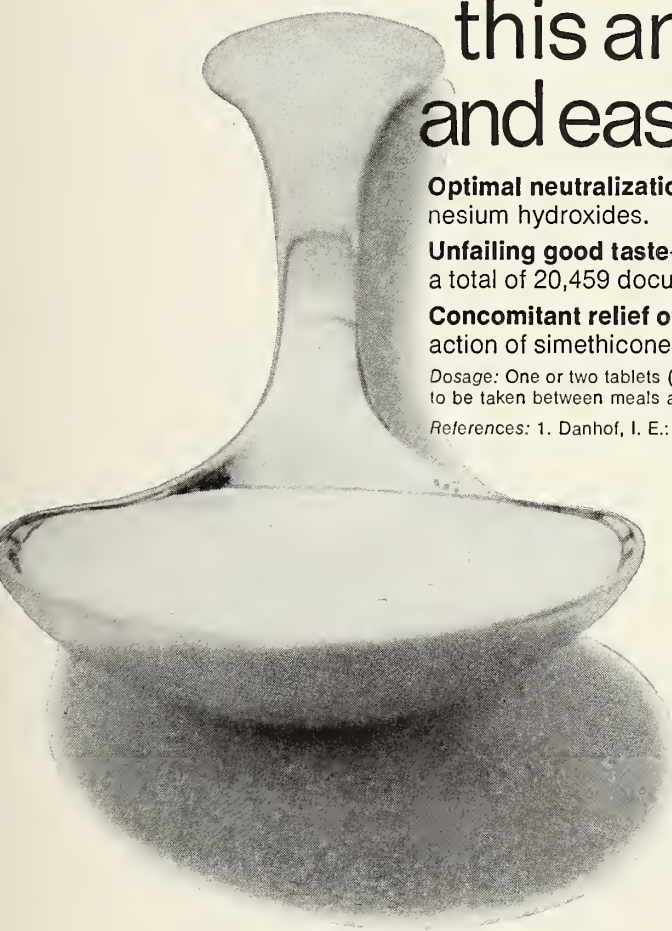
Dosage: One or two tablets (well chewed or allowed to dissolve in the mouth); one or two teaspoonfuls to be taken between meals and at bedtime, or as directed by physician.

References: 1. Danhof, I. E.: Report on file. 2. Hoon, J. R.: Arch. Surg. 93:467 (Sept.) 1966.

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farm applications of the chemical and a related one, DDD. The Wisconsin Natural Resources Department is considering a state wide DDT ban. Also the U. S. Agriculture Department has suspended use in its spraying programs of nine persistent insecticides including DDT. The New York City Parks Department have forbidden the use of DDT.

With biological warfare against insect pests a near reality, it is past time for special interests in the chemical industry to drop their outworn arguments about the usefulness of DDT in increasing production of crops, timber and livestock. With the perils of "hard" chemicals in mind the National Audubon Society has launched a campaign for a nationwide ban on DDT. While this broad and rational approach does not touch the global aspects of the problem, it would reduce the immediate danger in the United States and force substitution of less harmful chemicals and biological agents in the war on insects and disease.

L.H.N.

References

1. Burt Schorr: Replacing DDT. Wall Street Journal, July 31, 1969.
2. Time to Stop DDT is Now. New York Times, July 7, 1969.

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Teen-age Smoking In New Haven

I. Results of an In-Depth Survey

Ira S. Goldenberg, M.D. and Bernard Stoll, Ph.D.

Summary

A questionnaire administered to 5,259 New Haven, Connecticut junior and senior high school students revealed that almost one-third of them were cigarette smokers. Three of four smoking students had started by age 15 and one-third of them used more than ten cigarettes daily. Most of the teen-agers started to smoke as an experiment, found smoking enjoyable and continued the habit. Relaxation was the commonest end-point of smoking for the youngsters polled. Parental smoking habits and their approval or disapproval of children's smoking little influenced the latter.

The steady increase in the incidence of lung cancer has focused attention on this major public health problem during the past decade. The cause or causes of pulmonary malignancy have not been proven unequivocally but both cigarette smoking and air pollution have been profoundly implicated. The Surgeon General's Report of 1967, *The Health Consequences of Smoking*,¹ emphasized the position of the United States Public Health Service and incriminated tobacco again as the chief cause of lung cancer. A causal relationship has been denied by the tobacco industry and it is obvious that a great deal of definitive research must be done in both laboratory and clinic before the interrelations can be defined precisely. In the interim, we face the fact that cigarette consumption was almost 600 billion in 1968 while almost 59,000 Americans will die of lung cancer in 1969.

If one accepts the premise that lung cancer is linked to cigarette smoking, control of the disease must be related, at least in part, to reduction of cigarette use. The authors believe that cigarettes are responsible for the development of lung cancer in many individuals and the present study attempts

to define aspects of the smoking habit in a student population.

Any program to reduce cigarette consumption can be designed only after critical examination of the total population involved. Few smokers would deny that addiction to tobacco is a reality in most adult smokers, but past attempts to "break" such individuals of the habit have not been too successful. Much of the reason for this failure is the fact that these people have smoked for many years and such long term exposure is almost impossible to reverse. A more fertile field for smoking control might be among young people in whom the habit often is not yet fixed and in whom reversal may be possible.

How many youngsters smoke? What are their habits and motivational patterns? What are their backgrounds? What are their interests? Do they differ from non-smokers of the same age in any of these factors? An evaluation of these questions might offer clues as to whom smokes and why, and further, might enable design of an educational program with prospect of success in reducing cigarette smoking.

This study of a teen-age population in New Haven was undertaken to explore these queries. Previous questionnaire studies of a similar type have been done in several American communities,^{2,3} but most have been somewhat superficial and the results, although helpful, of limited value. An in-depth questionnaire was designed for this investigation which was easy for the student to complete, and which avoided ambiguity and maintained anonymity.

Methodology

The Education Steering Committee, New Haven Unit, American Cancer Society, designed the multiple-choice questionnaire to include both facts about and opinions of the individual completing it. A typical cross section of the urban New Haven teen-age population was chosen for examination in 3 public high schools and 3 junior high schools.

DR. IRA S. GOLDENBERG, Professor of Clinical Surgery, Yale University School of Medicine, New Haven.

DR. BERNARD STOLL, Assistant Professor, Department of Speech, Southern Connecticut State College. Dr. Stoll worked on this project in his capacity as chairman of the Education Committee, New Haven Unit, Connecticut Division, American Cancer Society.

Supported by the Henry A. Rudkin Memorial Fund, Yale University.

EDUCATION STEERING COMMITTEE, NEW HAVEN UNIT, AMERICAN CANCER SOCIETY

Introduction: This is a confidential questionnaire. No one will know who filled it out. It is very important that you answer each question truthfully and to the best of your knowledge. We thank you for your cooperation in this study. Directions: Be sure to answer each question. Give only one answer for each numbered question by checking the appropriate box or writing in the required answer.

- 1-4 Date Month Day Year
5-6 School
7 Grade
8-9 Age at last birthday
10 Sex: 1 Male 2 Female
11 What are your plans after graduation from high school?
12 What is your father's highest educational level?
13 Check only one of the following statements:
14-15 How old were you when you began to smoke?
16 Why did you start? Check only one of the following statements which best describes your reason:
17 What does smoking do for you? Check only one of the following statements which best describes your feelings:

- 18 If you smoke, does your mother or father know you smoke?
19 If you smoke, do your parents approve?
20 If you smoke, do you want to give it up?
21 If you were a parent, would you want your children to smoke?
22 Do your parents smoke?
23 Do any other members of your immediate family smoke?
24 Did your father ever smoke and stop?
25 Did your mother ever smoke and stop?
26 If you were a smoker and have given it up, check only one of the following statements which best describes your reason for giving up smoking:
27 Are you a member of a sports team?
28 Are you a member of a school club?
29 Are you a member of an outside social club?
30 Are you a member of a church group?
31 Have you ever held office in any group?
32 Do you believe smoking is dangerous to health?
33 Do you think smoking affects your ability to participate in sports?
34 Do you think smoking can shorten a person's breath?
35 Do you believe smoking can cause any diseases?
36 Lung cancer?
37 Heart disease?
38 Emphysema?
39 Tuberculosis?
40 If you were convinced that smoking would affect your health, would you stop?

CHECK TO BE SURE THAT YOU HAVE ANSWERED ALL THE QUESTIONS BEFORE HANDING IN THE QUESTIONNAIRE.

Figure 1—A reproduction of the questionnaire used in this survey.

Thus an age range of 11 through 21 including grades 7 through 12 was encompassed in a group of 5,259 completed questionnaires. Fewer than 1% of incomplete or inappropriately completed forms were eliminated. School officials and teachers cooperated and strict anonymity was assured on completed forms by limiting identification to age and sex of the student.

The questionnaire included details regarding the age when smoking started and the reasons for starting; extent of smoking at the time of the survey; the student's plans for the future; the family background, including smoking habits; parents' knowledge of the student smoking; student extra-curricular activities; opinions regarding the dangers of smoking; and if the student had stopped smoking, why the habit was discontinued. It was anticipated that the crude data might define local teenage smoking traits, but it was hoped, in addition, that study of the interrelations between social factors and smoking habits might provide insight into the make-up of these students as the basis for an improved educational campaign to discourage the habit. The questionnaire was prepared so that data processing cards and computer analysis could be used for data compilation. Fig 1 is the questionnaire in entirety.

Results

Smokers

Slightly less than 30% (1,555) of the total group of students completing the questionnaire admitted to smoking more than 3 cigarettes weekly. They were almost evenly divided between boys and girls and will constitute "smokers" in the present discussion. One-third of these students (461) stated that they smoked 10 or more cigarettes daily. Eighty-one per cent of the smokers had one or both parents smoking, but 34% of their fathers and 30% of their mothers had discontinued using cigarettes prior to the study. Ten per cent of smoking students would have no objection to their own children smoking, but 51% were not in favor of it.

One-third (30%) of smokers were members of an athletic team while 44% were active participants in other extra-curricular activities. Almost three-quarters (74%) of the students believed that smoking was dangerous to health; 66% thought smoking affected ability to participate in sports; 78% believed that smoking "can shorten a person's breath"; 77% thought that smoking can cause disease, especially lung cancer. Two-thirds (67%) of the students said they would stop smoking if they

were *convinced* that smoking would affect their health.

Age Started to Smoke

Almost one-third (31%) of the smoking group commenced the habit by the age of 12 with boys predominating in this early-start group. By age 15 three-quarters of the smoking students had started. There was no relationship noted between the age of smoking start and the fact that the immediate family members also smoked or what the students derived from smoking. It made little difference when the smoking started in reference to the student's opinion as to whether his parents knew about the activity. An interesting finding was that those who started smoking before age 14 were more often aware that their parents knew they smoked (82%) than those who started smoking later (18%). Participation in extra-curricular activities and opinion regarding the effects of smoking in relation to sports ability and health were not related to the age of smoking start. Almost half (43%) of those who felt that smoking is not dangerous to health started smoking at age 12 or less while fewer than a third (30%) of those who recognized the dangers of smoking started so early.

Why Started to Smoke

The commonest reason given for starting the smoking habit was "trying a cigarette and liking it" (46%). The influence of friends who already smoked started 14% of the students and, of interest, an additional 14% could give no reason for starting. Two-thirds of those who tried smoking and liked it felt that cigarettes relaxed them and they also liked the taste. Fewer than 3% reflected the influence of tobacco advertising as a reason for starting to smoke.

What Smoking Does for the Smoker

Over one-third (39%) of the students felt that relaxation was the end-point of their smoking. Only 14% liked the taste of cigarettes. Satisfaction was achieved in an additional 9% and another 7% used a cigarette "to give my hand something to do". A greater percentage of students found relaxation in smoking when their parents knew they smoked (84%) than when the students thought that their parents did not know of the habit (16%). Parental approval or disapproval did not seem to be related to achieving relaxation. No relationship was noted between parents' smoking and what smoking accomplished for the student.

Father's Educational Level

Fathers who attended or graduated from college comprised 16% of the smoking group while fathers attending school through the eighth grade or less were 14% of the group. Approximately the same percentage of fathers of smokers who started smoking at age 12 or less attended or graduated from college (20%) as attended school through the eighth grade or less (24%). A similar lack of relationship was noted between father's educational level and the following: the student's feelings about what smoking does for him; the reasons for starting to smoke; parents' knowledge or approval of smoking; the students' desire to stop smoking themselves or have their children start smoking; the student's belief that smoking is dangerous to health.

Parents' Knowledge and Approval

Seventy-one per cent of smoking boys and 63% of smoking girls said their parents knew they smoked. There appeared to be no relationship between parents' knowledge and student participation in extra-curricular activities. When parents knew of the student smoking, the youngsters more often wanted their own children to smoke than not (72% vs 63%). When parents did not know of their smoking, there was a greater tendency for the students to want their own offspring not to smoke than to adopt the habit (24% vs 12%). Parents' smoking habits past or present were not related to their knowledge of the student's use of cigarettes.

Parental disapproval existed in slightly greater than half (55%) of the total group. Such disapproval of smoking was greater among college-attending fathers (59%) than among fathers with less than an eighth grade education (48%). When parents disapproved, a larger portion of the students did not want to quit smoking (61%) than when parents approved (19%). In the group of students who wanted to stop, parental approval made a difference only among the girls where 29% wanted to stop when parents approved of smoking and 53% wanted to stop when parents disapproved.

More often than not, students who wanted their own children to smoke had parental approval of smoking (53% vs 36%). When parents disapproved, students overwhelmingly did not want their own children to smoke (67% vs 16%). Disapproving parents were usually non-smokers (62%), but when at least one parent smoked, disapproval still was present in over half of the group (52%). Approximately half (54%) of formerly smoking parents disapproved of student smoking.

Plans after Graduation

Slightly less than half (41%) of the smokers planned to attend college, while 24% planned to go to work. There was no relationship between post-graduation plans and the age at which smoking started. Relaxation was the main effect of smoking in both college and work groups (44% and 38% respectively).

Desire to Stop Smoking

More than one-third (38%) of smokers wanted to stop smoking. Those students who expressed a desire to stop were involved in extra-curricular activities more than those who did not want to stop (38% vs 30%). Parents were more often aware of the student's smoking in the group that wanted to stop than in the group that did not want to "break the habit" (21% vs 12%). When one or both parents smoked, 38% of the students wanted to stop themselves while only 28% had no desire to stop. The desire to discontinue smoking was even greater when neither parent smoked (42% wanted to stop and 27% did not). When either parent had previously discontinued the use of cigarettes, 41% of the students polled wanted to quit while 28% did not want to stop.

Non-Smokers

Only 36% of the 3,704 non-smoking students completing the questionnaire stated that they had never smoked at any time. Thirty-seven per cent of non-smokers were members of an athletic team and 48% participated in other extra-curricular activities. Almost all of the non-smokers (90%) believed that smoking is dangerous to health; 81% felt that smoking affects sports ability; 81% thought that smoking "shortens breath"; 89% believed that smoking is associated with causation of disease, especially lung cancer. If *convinced* that smoking affects health, 95% of the non-smoking students said they would not start to smoke.

Seventy-six per cent of non-smokers had one or both parents currently smoking. One-third (32%) of non-smokers' fathers had smoked at some time and had stopped, while 29% of their mothers had discontinued the habit. Eighteen per cent of the fathers of non-smokers attended or graduated from college while 14% of the fathers had an eighth grade education or less. Only 2% of non-smoking students wanted their children to smoke and 80% said they would not approve of such activity.

Over half (56%) of the non-smokers planned to attend college and one-sixth (16%) contemplated

work after graduation. Desire to be "a better athlete" was the main reason given by male students for discontinuation of smoking prior to the survey (19% of the group) with recognition that smoking was "bad for health" the commonest reason for both boys and girls (21%) irrespective of post-graduation plans.

Comment

This study defines several features of the teen-age population in relation to smoking and has reemphasized factors previously described by other investigators. The prevalence of smoking among teen-agers is well known and there is a significant segment initiating the habit at an early age and smoking a large number of cigarettes daily. Many studies have indicated that this group is at great risk because the duration of excessive smoking may be related to the development of cardiorespiratory pathology, especially lung cancer. It is, therefore, imperative that educational efforts be directed toward the population less than 12 years of age and indoctrination about the health hazards of smoking should be started at age 5 or 6 when formal schooling begins. Too little effort has been expended by health agencies in this sector.

Parental smoking habits and opinions about smoking have been mentioned as influences in the development of the teen-age smoker. The present study has demonstrated little difference, however, in the number of smoking parents between the groups of young smokers and non-smokers. It might be presumed that the presence of adult smokers in the household would prompt children to start smoking at an earlier age than when children were not exposed to family smokers, but such was not noted here. The percentage of parents who had discontinued smoking was approximately the same among teen-age smokers and non-smokers. Further, it is attractive to postulate that better educated parents, especially those with exposure to college, might have more influence on their children's smoking habits than parents who had less education. If the educational level of fathers is an indication, such an influence was minimal here. A greater degree of disapproval of student smoking was noted among college fathers and such disapproval did have some effect on student opinions in that such youngsters did not want their own children to smoke. Generally speaking, however, parental pressures seem to be small as related to teen age smoking and perhaps have been overemphasized in the past.

Does group conformity play a role in developing young smokers? Such pressures on the individual

have been noted previously, but in the group under examination here only 20% of the students felt so influenced by friends or the fact that "everyone does it". Such mechanisms as "a dare", wanting a "new kick" or the influence of advertising were unimportant in starting young smokers. The commonest reason for starting to smoke must be categorized as experimental on the part of the youngster who then obtained some satisfaction from the trial and thereafter continued the activity.

The stresses and strains of modern living reach even into the lives of the junior and senior high school students surveyed here. Relaxation, e.g. from tension, was the commonest end-point of smoking noted. Both smokers and non-smokers were equally active in extra-curricular activities, but such undertaking obviously did not provide an adequate outlet for tension. It can only be postulated that the development of other types of programs than currently exist within the school environment or outside the school milieu might "soak up" excess energy and possibly decrease the need for cigarettes as a form of relaxation.

The addictive power of smoking is perhaps best illustrated by the fact that 74% of smokers believed that smoking is dangerous to health, yet only a third (38%) wanted to stop smoking. The students seemed unable to relate the dangers of smoking to their own habituation. This finding suggests immaturity of judgment, but other student opinions reflected reality in that, for example, smokers and non-smokers alike preferred that their own children not smoke (57% and 80% respectively).

This study clearly demonstrates that smoking teen-agers differ little from non-smokers in the several aspects surveyed. Certainly other factors may be important and analysis of psychological implications will be the topic of a further study. Several points are clear at this time:

1. Three-quarters of teen-age smokers are habituated by age 15, the majority to the point of intellectual negation of the health hazard involved. Thus, education to emphasize the relationship between smoking and disease must start early enough for prevention, perhaps even in kindergarten.
2. Parental influences seem minimal and efforts to change teen-age smoking patterns through adult education will be unproductive.
3. Smoking evidently serves as a mode of relaxation from present day tensions for the teenager as well as the adult and study of this fac-

tor in the school and home environment may give some clue to possible less lethal substitutes for the cigarette.

Members of the Education Steering Committee, New Haven Unit, Connecticut Division, American Cancer Society in addition to the authors: Dorothy Kirk, Lillian Konick, John McGavack, Jr., Charlotte Smith, Ned Thomas.

References

1. The Health Consequences of Smoking, A Public Health Service Review: 1967, U. S. Government Printing Office, Washington, 1968.
2. Andrus, L. H., Hyde, D. F. et al: Smoking by High School Students, *California Medicine* 101: 246-7, (October) 1964.
3. Jensen, L. M., and Thompson, J. C.: Report of 1965 Smoking Survey, Lincoln Public Schools—Senior High Schools, *Journal of School Health* 35: 366-373, (October) 1965.

Psychiatric Referral For Teen-Ager Drug Users

What are your indications for referring a teen-ager who is a drug user to a psychiatrist?

“I think that one of the main danger signs in dealing with adolescents is depression; which is, after all, sometimes the precursor to suicide. . . . In talking with young people, I think one should gauge the depth of the depression carefully and face up to the issue of suicide. . . . The young people aren't afraid to talk about suicide. Some of them enjoy talking about it, and these are probably the ones that you need to worry less about. The ones who express real worry about what they may do to themselves and who are contemplating some particular method of committing suicide certainly should be referred immediately for some kind of psychiatric help.

“[Two other considerations are important in thinking about referral.] One is if you feel that you're not communicating with your patient—that you don't understand what he is saying, or you're on another wave length, or somehow you're not meeting—this is a reason to refer. It may just be that he doesn't like you very much; but it may also mean that he feels unhappy because he hasn't made contact, and this may make him more frustrated and more desperate. The other thing, which is a clue, is your own anxiety level. If you're talking with a patient, and for some reason he makes you very nervous and upset and scared and you start dreaming about him at night, this is a good reason to get somebody else to see him and size up the situation.”

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The Direct Agglutination Pregnancy (DAP) Test

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Immunologic tests for pregnancy have largely supplanted animal tests because of their accuracy and convenience. The immunologic tests are based on observation of a visible reaction between human chorionic gonadotropin (HCG) and antibodies to the HCG. With two exceptions^{1,2} the reactions have been indirect in that agglutination occurs if the patient is *not* pregnant and agglutination does not occur if she *is* pregnant. A new direct test entitled DAP (Direct Agglutination Pregnancy) in which agglutination occurs if the patient is pregnant was submitted to us for evaluation by its manufacturers*.

Principle

The indirect tests are carried out as follows. Test urine is added to anti-HCG serum. If HCG is present in the urine the antiserum is neutralized; if HCG is absent the antiserum retains its potency. Particles sensitized with HCG are then added. If the antiserum is still potent the particles undergo visible agglutination; if the antiserum has been neutralized there is no agglutination.

The direct test employs a reagent consisting of antibody to HCG (anti-HCG) absorbed on latex particles. When this material is added to urine containing HCG the particles agglutinate, so that agglutination indicates pregnancy.

Performance of the DAP Test

The urine must be cooled to room temperature and filtered through fine filter paper such as Whatman #42. The DAP reagent is also brought to room temperature and shaken thoroughly. The glass slides with marked circles are washed before use

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* Wampole Laboratories, Stamford, Conn.

each time with detergent, rinsed several times in distilled water and wiped dry with lint free tissue.

1. The capillary tube is filled to the mark with filtered urine; this is expelled into the circle on the slide.

2. 1 drop of the DAP Test reagent is added to the circle and mixed well over the entire circle with the stirrer provided.

3. The slide is rocked gently and slowly for 2 minutes and then read for agglutination.

4. Agglutination occurs if the urine contains HCG.

Agglutination is easily read by fluorescent light. Positive reactions are readily recognized because the clumps are quite definite and coarse.

Precautions

The DAP test should not be performed on freshly voided warm unfiltered urine. 10 urines from non-pregnant women aged 23 to 50 years *all* gave false positive DAP tests, true negative UCG tests when the specimens were tested immediately after voiding. The same samples were correctly negative after cooling and filtration.

Material and methods

130 consecutive urine specimens brought to the Norwalk Hospital Laboratory for routine pregnancy testing were studied between September 12, 1967 and June 6, 1968. Both an indirect test (UCG*) and the direct (DAP) tests were performed. After suitable intervals we made written inquiry of the attending physicians to determine whether the patient had been pregnant at the time of the test and also the outcome of the pregnancy. Additional checks were carried out by reviewing the hospital charts if the patient had been admitted subsequent to the test.

The results are tabulated below.

TABLE 1
RESULTS FROM UCG AND DAP TESTS, 130 SPECIMENS

<i>Test Results</i>	<i>Pregnant</i>	<i>Not pregnant</i>
Both tests positive	74	1 ^a
Both tests negative	2 ^{bc}	52
UCG positive, DAP negative	1 ^d	0
UCG negative, DAP positive	0	0
	77	53

a—48 year old woman. No medication.

b—test date 9/12/67; delivered 5/24/68.

c—test date 6/12/68; clinical EDC 2/5/69. Patient bleeding at time of test, subsequently stopped and pregnancy progressed normally.

d—patient aborted 2 days after test performed.

This can be expressed in percent accuracy as follows:

TABLE 2

<i>Classification</i>	<i>UCG</i>	<i>DAP</i>
True positive	97.4%	96.1%
True negative	98.1%	98.1%
False positive	1.9%	1.9%
False negative	2.6%	3.9%

The UCG results are similar to those in a previous series of 93 cases we studied in 1963 in which we found 96% true positives and 100% true negatives. The DAP results are almost identical. The one negative DAP positive UCG in a woman about to abort reflects the greater sensitivity of the UCG, 1 IU/ml, vs 2 IU/ml for the DAP. Our results are essentially the same as those previously reported for UCG and other indirect tests³⁻⁹ and for a direct test.^{1,2} These results range for routine clinical material about 95% true positive and 2% false posi-

tive, although a higher percentage of true positives can be achieved for selected normal pregnancy urine 2-3 weeks after the first missed menstrual period.

Summary and conclusions

In a series of 130 consecutive urine pregnancy tests a new direct immunologic pregnancy test (DAP) demonstrated a high level of sensitivity (96% true positives) and of specificity (1.9% false positives), comparable to those expected with the indirect tests. It is rapid (2 minute observation) and easy to read. Prior chilling and filtration of the urine specimen is essential.

References

1. Fink, H. and Fric, A. A rapid direct-reading latex agglutination pregnancy test. *Obs. and Gyn.* 28, 660-662, Nov. 1966.
2. Graham, M. A. and Kalish, P. E. A comparison of a new latex agglutination pregnancy test with an established latex agglutination-inhibition test; *A. J. Clin. Path.* 47, 100-104, Jan. 1967.
3. Bonsnes, R. W. and Marney, A. F. Accuracy of a passive hemagglutination inhibition method for the determination of chorionic gonadotropin in the urine. *A. J. Obs. Gyn.* 98, 208-214, May 15, 1967.
4. Davajan, V. and Mishell, D. R. Comparison of immunologic determinations of HCG in urine and in serum. *Obs. and Gyn.* 29, 515-519, April, 1967.
5. Goetschel, E. Evaluation of a new immunologic pregnancy slide test. *A. J. Ob. Gyn.* 99, 1101-1105, Dec. 15, 1967.
6. Mendel, E. B., Haberman, S. and Zimmerman, E. Evaluation of two rapid immunologic tests for pregnancy. *Obs. and Gyn.* 26, 207-210, Aug. 1965.
7. Noto, T. A. and Miale, J. B. New immunologic test for pregnancy. A two-minute slide. *A. J. Clin. Path.* 41, 273-278, Mar. 1964.
8. Reynolds, J. B. Immunologic pregnancy tests—their potentialities and limitations. *Oklahoma State Medical Association Journal* 57, 245-250, June 1964.
9. Thompson, R. B., Mayo, R. W. and Bell, W. N. A critical evaluation of pregnancy tests, biologic versus immunologic. *A. J. Clin. Path.* 47, 585-590, Nov. 1965.

Surgery For Coronary Occlusive Disease

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One of the greatest challenges that clinical surgery and surgical research faces today is the development of an effective, safe armamentarium of surgical procedures for the treatment of coronary occlusive disease. In 1966, the United States vital statistics³⁹ lists death from coronary artery disease at 365.8/100,000 population and death from cancer at 151.3/100,000 population. Therefore, death from heart disease, of which coronary artery disease makes up the vast bulk, is not only first, but first by over two times the second major cause of death. These figures have not been improved despite therapeutic advances and judicious medical management on the part of cardiologists, internists and general practitioners, and the sequelae of coronary artery disease—infarction, arrhythmias, congestive failure, and angina are as common today as they were 25 years ago.

Until the etiology of atherosclerosis is understood and its prevention established on a biochemical basis, the treatment of obstructed and calcified coronary arteries will fall, in appropriate cases, to the ingenuity and imagination of surgeons. The dramatic ascendancy of cardiac and vascular surgery in the past fifteen years has provided the refinements in technique and equipment which now make coronary reconstructive surgery a reasonable possibility. Combined with this advance is Mason Sones' major contribution of selective coronary cineangiography,³⁷ which has finally changed the surgery of coronary artery disease from the treatment of a symptom, angina, to the treatment of demonstrable pathology.

The first surgical procedure for the relief of angina was cervical sympathectomy, proposed by Jonnesco²³ in 1922. This operation successfully blocked transmission of painful stimuli but probably did little to correct the basic disease. In 1933 Blumgart, Levine, and Berlin⁷ advocated total thyroidectomy to lower body metabolism and thereby decrease cardiac work and lessen or eliminate angina. This

procedure, unfortunately, left patients with all the unpleasant side effects of hypothyroidism while doing nothing to correct the underlying pathology. Because of these drawbacks thyroidectomy never gained general acceptance. In 1935 the concept of relieving angina by increasing myocardial blood supply was advanced by Beck³ when he sutured a pedicle of pectoralis major muscle to the heart after removal of the epicardium. This concept started a series of "pexy" operations by other investigators and included O'Shaughnessy's cardioomentopexy,²⁷ Carter's cardiopneumopexy,⁸ Thompson and Raisbeck's cardiopericardiopexy,⁴⁰ and Key's cardiojejunopexy.²⁴ Although vascular communications with the heart could usually be shown after these procedures, they were always of minute size and the direction of blood flow could never be adequately demonstrated. In 1941 Beck and his associates observed that removal of the epicardium from dogs' hearts increased intercoronary anastomoses formation,³⁸ and in 1943 he noted a similar effect when irritant materials were applied to the surface of the heart.³³ Beck incorporated these observations into an operation which is referred to as the Beck I procedure and which includes epicardiectomy, asbestos administration to the heart, pericardial fat pad application to the myocardium, and partial narrowing of the coronary sinus. In 1958 Beck reported⁴ that this procedure had been performed on 347 patients and that 94% of the 295 survivors experienced relief of anginal pain. Despite the high incidence of relief from symptoms the procedure has appeared unphysiologic to many surgeons, and since the volume of new blood entering the myocardium and its oxygen-carrying ability could not be quantitated the procedure has not gained general acceptance.

In 1948 Beck devised what became known as the Beck II procedure.⁵ This operation established a shunt between the aorta and coronary sinus, thereby delivering arterial blood in antegrade fashion to the right atrium and in retrograde fashion to the venous side of the myocardial circulation. It was hoped that this procedure would make large amounts of blood continuously available to the heart despite progression of obstructive disease on the arterial side of the myocardial circulation. Bailey's review¹ of Beck's patients who underwent

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this procedure shows an operative mortality of 20% and an improvement in symptoms in 80% of survivors. The Beck II procedure undoubtedly increased blood supply to the heart initially, but unfortunately it also developed a sizable arteriovenous fistula with resulting increased metabolic demands on the myocardium. In addition Eckstein and Leighninger² have shown that the arterial pressure produces a marked intimal hyperplasia on the cardiac veins with cessation of flow five weeks after shunt. Because of these drawbacks and the high operative mortality rate the Beck II procedure is no longer employed.

Today myocardial revascularization is following two separate approaches: The first attempts to bring extracoronary blood to the heart without directly disturbing the coronary arteries and is particularly useful in treating diffuse or small vessel disease, and the second involves surgery directly upon the coronary arteries themselves and is designed to remove or bypass segmental occlusions in the larger, proximal coronary arteries.

The majority of people afflicted with coronary disease suffer from a diffuse type of atheroma which is seen pathologically as multiple obstructing and partially obstructing lesions scattered throughout the coronary tree. Because of the difficulty of re-establishing the patency of the entire coronary vasculature, it has fallen to the ingenious attempts of investigators to establish other means of bringing new blood to the myocardium. The most commonly used procedure today is the internal mammary artery implant.

In 1946 Vineberg discovered that the freely bleeding internal mammary artery remained patent when implanted into the myocardium. This has been a difficult concept for many to grasp, but it has been proven by a considerable number of surgical investigators.^{6,13,32} Vineberg's explanation⁴³ of why the artery is able to stay open without hematoma is based on Wearn's findings⁴⁶ of numerous myocardial sinusoids which communicate with the capillary bed and ventricular lumina. Vineberg theorized that blood egressing from the acutely implanted internal mammary artery drains off through the myocardial sinusoids until it is able to establish communications with the existing coronary arteries.⁴²

The results of the internal mammary artery implant procedures were published in 1964 by Vineberg and Walker.⁴⁵ They report, in their combined series on 140 patients, an operative mortality of 5%. Postmortem injection studies of 18 hearts from pa-

tients that died from eight hours to four years post-operatively showed an internal mammary artery implant patency rate of 78%, and 83% of survivors reported an improvement in symptoms.

Until recently there has been little work published on the physiology of the internal mammary artery implant, and such questions as whether it carries a significant amount of blood to the heart and whether this blood contributes to cardiac metabolism have been clouded issues. Flowmeter studies of acute and chronic internal mammary artery implants in dogs with ameroid-induced anterior descending artery ischemia have been performed in our laboratory.³⁰ These studies show that the acutely implanted internal mammary artery has a mean flow rate of approximately 5 cc. per minute and a pulsatile tracing which is greatly altered from the normal, in situ internal mammary artery. The acute implant demonstrates marked fluctuations in forward and reverse flows during each cardiac cycle while the in situ artery demonstrates the typical flow tracing of any systemic artery. Studies on animals from one week to eight months postimplant show that the flow rate of 5 cc. per minute remains relatively constant for the first six weeks and then rises gradually until six months after implant. At this point it plateaus at about 30 ml. per minute which approximates but does not quite equal the flow in a normal anterior descending artery of a 15-kg. dog (Fig. 1). It is of interest

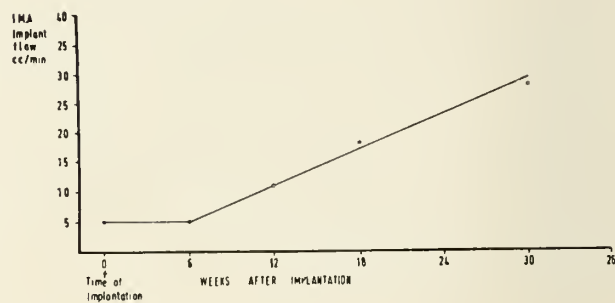


Figure 1

The graft shows the increase in flow over a 30-week period of internal mammary artery implants implanted into the ischemia myocardium.

that pulsatile tracings of the implant at this time closely resemble the pulsatile tracings of a normal coronary artery, i.e., maximal forward flow occurring during diastole and greatly reduced flow occurring during systole. This, of course, is the reverse of the flow pattern which is obtained from a normal systemic artery. The response of the internal mammary artery to coronary vasodilators six months after im-

plant was also studied and compared with the effects of these drugs on systemic flow. It was seen that amyl nitrite and levarterenol markedly increased internal mammary artery implant flow while decreasing systemic artery flow, again demonstrating that the internal mammary artery implant, once it has established enough collaterals with the existing coronary tree, behaves like a coronary artery and quite the reverse of a systemic artery. If the implanted artery is transected with the heart beating in situ and the blood which egresses from the distal cut end is studied for oxygen and carbon dioxide concentrations, it can be demonstrated that this blood compares similarly with systemic arterial blood. This clearly shows that the back-bleeding is arterial rather than venous in nature and therefore justifies the statement that the internal mammary artery implant makes connections with the arterial side of the circulation rather than the venous side.

It is unlikely that implant flow will equal anterior descending flow, even when the latter vessel is completely occluded, since some anterior descending demand will be replaced by anastomoses with the circumflex and right coronary arteries. However, the total sum of blood entering the anterior surface of the myocardium after implant is probably equal to what a normal anterior descending artery contributes. The significant fact is that the additional blood which the implant brings into the ischemic myocardium is supplementary to the basic coronary flow and does not entail redistribution of this blood at the expense of other areas of the myocardium.

Gorlin and Taylor¹⁸ have shown that the clearance curves of radioactive Krypton (85 Kr.) injected into internal mammary artery implants and the left ventricle of human patients are similar and indicate that the isotope is cleared in the same manner by the coronary arteries and the internal mammary artery implant. This evidence gives further support to the fact that the implant makes communications with the arterial rather than the venous system. These investigators also demonstrated, through determinations of myocardial lactate extraction, that in 6 of 9 postimplant patients the heart had shifted from anaerobic to aerobic metabolism. These important findings give much support to Vineberg's initial premise that the internal mammary artery implant is capable of performing the work of a normal coronary artery.

In an effort to decrease the incidence of implant occlusion, which has been reported in the literature—22% in Vineberg's series⁴⁵ and 15% in Effler's series¹⁶—Sewell has proposed the pedicle implant.³⁶

In this procedure the internal mammary artery is dissected from the chest wall along with the internal mammary vein and surrounding muscle and fascia. The pedicle is then implanted into the anterior myocardium beneath a major branch of the anterior descending artery. Sewell feels that flow in the acutely implanted pedicle will be higher than in a standard internal mammary artery implant because capillary communications between the internal mammary artery and internal mammary vein are already present in the surrounding tissue of the pedicle; therefore blood in the artery will have an established drainage pathway. Sewell³⁴ has obtained internal mammary artery implant arteriograms on 57 patients and reports a closure rate of only 5%.

By slightly modifying Vineberg's technique we were able to achieve a 100% patency rate of the internal mammary artery implant in the experimental animal.^{21,30} Vineberg's technique⁴⁵ consists of dissecting the internal mammary artery from the fourth to the sixth interspace and then implanting the artery in the myocardium while freely bleeding from its side branches. With our modification the internal mammary artery is dissected from a point on the chest wall opposite the apex of the heart to its origin at the subclavian artery. It can then be laid along the great vessels and base of the heart and implanted in a somewhat longer tunnel. We feel this modification has the following advantages: (1) The artery is not angled as it leaves the chest wall and then angled again as it enters the myocardium. (2) The artery is not attached to the anterior chest wall causing it to pivot around a fixed point with each heartbeat. (3) No proximal branches are left between the implanted portion of the internal mammary artery and its origin at the subclavian artery; therefore the force of systemic pressure is directed entirely toward driving blood into the myocardium rather than being shunted out proximal intercostal branches to supply the anterior chest wall. We believe that the two most important factors in keeping the acutely implanted artery open are the to-and-fro motion of the blood which occurs in the artery with each cardiac cycle and the small net forward flow which runs into the myocardial sinusoids.³⁰

An important consideration in maintaining internal mammary artery implant patency is sufficient myocardial ischemia. Provan²⁹ has shown that internal mammary artery implants in dogs which do not have induced anterior descending artery ischemia uniformly develop intimal hyperplasia which severely reduces the internal diameter of the im-

planted portion of the artery. In clinical practice the angiographic evidence for determining the necessary degree of ischemia varies from center to center. Effler's¹⁶ requirement is severe occlusive disease in the anterior descending artery, while Sewell³⁴ requires 75% or more occlusion in all coronary arteries, and Vineberg⁴⁵ advises complete occlusion of the anterior descending artery or 50% occlusion of the anterior descending artery and partial or complete occlusion of the circumflex coronary artery. Undoubtedly, as more experience is gained with coronary cineangiography and preoperative selection of patients, occlusion of the implant from this cause should be less of a problem.

As Vineberg's work has gained acceptance, other investigators have adopted his principle and modified his technique in efforts to revascularize portions of the heart not reached by the standard single internal mammary artery implant. Most of these procedures have dealt with methods of revascularizing the posterior surface of the myocardium. Bailey² has devised the gastroepiploic artery implant, in which he frees this artery from the stomach, brings it through the diaphragm, and tunnels it into the posterior surface of the heart. Urschel¹¹ has proposed the retrograde internal mammary artery implant. In this procedure the internal mammary artery is dissected from the chest wall, ligated and divided at its proximal end, swung below the apex of the heart, and implanted into the posterior myocardium. Pearce and Creech²⁸ propose the use of intercostal arteries which can be dissected from the chest wall and be implanted in various places in the left ventricular myocardium. Aorto-myocardial vein graft has been advanced by Deitrich⁹ and has received experimental evaluation in his laboratory. In this procedure a section of autogenous vein is anastomosed to the side of the aorta and tunneled into the anterior or posterior surface of the heart while bleeding from holes cut in its side. Unfortunately, the closure rate in the first two months is discouragingly high. The most common procedure now performed for triple vessel disease including posterior wall ischemia is the double internal mammary artery implant; one vessel being implanted into the anterior surface of the left ventricle and the other into the posterior, or diaphragmatic, surface of the left ventricle. It has become apparent, as more surgical experience is gained, that the left internal mammary artery can be swung easily underneath the heart and implanted posteriorly. The double internal mammary artery implant procedure has now obviated and

largely supplanted other methods for bringing blood to the posterior surface of the heart.

While the internal mammary artery implant procedure has been shown to be beneficial in many cases, it does have certain drawbacks. These drawbacks are associated with the inability of the internal mammary artery to increase myocardial blood supply at the time of surgery. Therefore, a heart which is already maximally stressed because of coronary artery disease is required to accept the extra metabolic load of major surgery and depressant effects of anesthesia and counter-myocardial irritant drugs. These factors account for the 8% operative mortality which is reported for this type of surgery and has stimulated surgeons to develop procedures which will increase blood supply immediately. These procedures involve the coronary arteries directly.

Direct coronary surgery, because of arterial size, is presently confined to the large proximal trunks and, theoretically, is no different from operating on vessels of comparable size elsewhere in the body. The methods employed clinically to relieve segmental occlusions have been coronary endarterectomy, coronary arteriotomy and patch graft angioplasty, coronary artery resection and vein graft interposition, vein bypass graft and artery bypass graft. In addition an unusual approach has been devised by Lary²⁵ and used successfully in one patient.

Longmire and Cannon have, perhaps, the widest range of experience with coronary endarterectomy. In a review of their clinical cases Dilley et al.¹⁰ report that the operative and early postoperative mortality without cardiopulmonary bypass was 58%, while with cardiopulmonary bypass it dropped to 23%. All cases of operative death occurred in patients having the left coronary artery or its branches operated upon. He also reported that three of four patients undergoing coronary endarterectomy who died in the early postoperative period had thrombosed endarterectomized segments. Finally four patients that died in the late postoperative period had a diffuse hyperplasia of the neointima with only minute openings remaining in the coronary arteries.

To circumvent the problems associated with endarterectomy,¹² Effler¹⁵ has proposed coronary arteriotomy with pericardial patch graft to relieve the point of obstruction. All his patients were maintained on cardiopulmonary bypass and regional hypothermia, but the myocardium supplied by the artery being operated upon was not perfused. In his latest series¹⁴ the overall operative mortality was

22%. The operative mortality for procedure involving the right coronary artery, however, was only 6%, whereas operations involving the left coronary artery showed a 53% mortality rate. While initial reports of this procedure were good, long term results have been disappointing. Favaloro¹⁷ reported a complete follow-up including selective coronary cineangiography on 180 patients. These studies showed that 13% exhibited significant narrowing and 29% had total occlusions at the site of the patch. This occurred most often in patients with long segmental occlusions. In an effort to improve these results Favaloro now resects the segment of occlusion and interposes a segment of saphenous vein graft. At this time, the total number of patients with whom this new operative technique has been applied is 55 with an operative mortality of 3.6%. A very respectable figure for this type of surgery and a significant improvement over other procedures. Bypass grafting of obstructive lesions in the coronary arteries has been performed by Johnson²² who uses a vein graft sutured to the side of the aorta proximally and to the side of a coronary artery distally. Green²⁰ also uses bypass grafts but instead of vein, has proposed and currently uses the internal mammary artery anastomosed directly to side of a coronary artery distal to the point of obstruction.

Lary's²⁵ recently presented techniques of relieving segmental occlusions consists of sewing a vein patch graft tent to the epicardium over the obstructed artery. Next a small automatic scalpel is advanced up a marginal artery and through the point of obstruction. The posterior wall of the artery is then laid open so that bleeding occurs freely into the substance of the myocardium and new lumen provided by the patch graft.

As in all types of surgery, it is apparent there remains room for improvement. It is important to realize, however, that 85% of patients undergoing internal mammary artery implant have received sufficient improvement that they return to work and lead normal lives. In addition, patients that have undergone successful direct procedures are immediately and completely relieved of symptoms and are able to return to a normal life with little or no restriction in diet or exercise. As more and more of these patients are referred to surgeons, techniques will be refined and results will improve; as this happens, it is inevitable that coronary reconstructive surgery will achieve the same level of proficiency that valvular and congenital cardiac surgery now enjoys and hopefully we will, in time, be able

to point at coronary artery disease as the number two cause of death in the United States.

References

1. Bailey, C. P.: *Surgery of the Heart*. Philadelphia: Lea & Febiger, 1955.
2. Bailey, C. P., Hirose, T., Brancato, R., Aventura, A., and Yamamoto, N.: Revascularization of the posterior (diaphragmatic) portion of the heart. *Ann. Thorac. Surg.* 2:791, 1966.
3. Beck, C. S.: The development of a new blood supply to the heart by operation. *Surgery.* 102:108, 1935.
4. Beck, C. S., Leighninger, D. S., Brofman, B. L., and Bond, J. F.: Some new concepts of coronary heart disease. *J.A.M.A.* 168:2110, 1958.
5. Beck, C. S., Stanton, E., Batiuchok, W., and Leider, E.: Revascularization of the heart by graft of a systemic artery or a new branch from the aorta into the coronary sinus. *J.A.M.A.* 137:436, 1948.
6. Bigelow, W. G., Basian, H., and Trusler, G. A.: Internal mammary artery implantation for coronary heart disease. *J. Thorac. Cardio. Surg.* 45:67, 1963.
7. Blumgart, H. L., Levine, S. A., and Berlin, D. D.: Congestive heart failure and angina pectoris—The therapeutic effect of thyroidectomy on patients without clinical or pathological evidence of thyroid toxicity. *Arch. Intern. Med. (Chicago)* 51:866, 1933.
8. Carter, B. N.: Discussion of Beck, C. S. Revascularization of the heart. *Ann. Surg.* 128:861, 1948.
9. Deitrich, E. B., Morris, J., Liddicoat, J., and Wessinger, J.: Myocardial revascularization: Evaluation of autogenous vein grafts between the aorta and myocardium. *Ann. Thorac. Surg.* 1:671, 1965.
10. Dilley, R. B., Cannon, J. A., Kattus, A. A., MacAlpin, R. N., and Longmire, W. P.: The treatment of coronary occlusive disease by endarterectomy. *J. Thorac. Cardio. Surg.* 50:511, 1965.
11. Eckstein, R. W., and Leighninger, D. S.: Chronic effects of aorta-coronary sinus anastomoses of Beck in dogs. *Circ. Res.* 2:60, 1954.
12. Effler, D. B.: Surgical procedures for relief of myocardial ischemia: Preliminary report. *Surgery.* 55:90, 1964.
13. Effler, D. B., Groves, L. K., Sones, F. M., Jr. and Shirey, K.: Increased myocardial perfusion by internal mammary artery implant: Vineberg's operation. *Ann. Surg.* 158:526, 1963.
14. Effler, D. B., Groves, L. K., Suarez, E., Favaloro, R. G.: Direct coronary artery surgery with enderotomy and patch graft reconstruction: clinical application and technical considerations. *J. Thorac. Cardio. Surg.* 53:93, 1967.
15. Effler, D. B., Sones, F. M., Favaloro, R., Groves, L. K.: Coronary endarterotomy with patch-graft reconstruction: Clinical experience with 34 cases. *Ann. Surg.* 162:590, 1965.
16. Effler, D. B., Sones, F. M., Groves, L., and Suarez, E.: Myocardial revascularization by Vineberg's internal mammary artery implant: Evaluation of postoperative results. *J. Thorac. Cardio. Surg.* 50:527, 1965.
17. Favaloro, R. G.: Saphenous vein autograph replacement of severe segmental artery occlusion. *Ann. Thorac. Surg.* 5:334, 1968.
18. Gorlin, R., and Taylor, W.: Revascularization of the myocardium by internal mammary artery implant. *New Eng. J. Med.* 275:290, 1966.

19. Gott, V. L., Whiffen, J. D., Koepke, D. E., Daggett, R. L., Boake, W. C., and Young, W. P.: Techniques of applying a graphite-benzalkoniumheparin coating to various plastics and metals. *Trans. Amer. Soc. Artif. Intern. Organs.* 10:213, 1964.
20. Green, G.: Bypass grafting of the coronary artery. Address to Yale University School of Medicine. February 18, 1969.
21. Hammond, G. L., Provan, J. L., and Austen, W. G.: Re-evaluation of myocardial revascularization procedures. *Ann. Surg.* 164:951, 1966.
22. Johnson, W. D., Harding, H., Lepley, D.: The aggressive surgical approach to coronary disease. Presented at the forty-ninth annual meeting of the American Association for Thoracic Surgery, San Francisco, Calif. April 2, 1969.
23. Jonnesco, T.: La resection du sympathique cervicothoracique "technique operative." *Presse Med.* 30:353, 1922.
24. Key, J. A., Kergin, F. G., Martineau, Y., and Leckey, R. G.: The method of planting the coronary circulation by jejunal pedicle graft. *J. Thorac. Surg.* 28:320, 1954.
25. Lary, B. G., Chesney, J. G., Gentsch, T. O. and Larson, P. B.: The "coronary myocardial artery" for coronary artery disease. *Dis. Chest.* 49, 412, 1966.
26. Nardi, G. L., and Shaw, R. S.: Emergency coronary endarterectomy. *Dis. Chest.* 44:193, 1963.
27. O'Shaughnessy, L.: Experimental method of providing collateral circulation to the heart. *Brit. J. Surg.* 23:665, 1936.
28. Pearce, C., and Creech, O., Jr.: Myocardial revascularization: Use of intercostal artery. Presented at the forty-sixth annual meeting of the American Association for Thoracic Surgery, Vancouver, B. C., May 18, 1966.
29. Provan, J. L.: Mammary-coronary anastomoses: A short histological study. *Brit. J. Surg.* 49:199, 1961.
30. Provan, J., Hammond, G. L., and Austen, W. G.: Flowmeter studies of internal mammary artery implantation into the left ventricular myocardium. *J. Thorac. Cardio. Surg.* 52:820, 1966.
31. Sabiston, D. C.: Coronary endarterectomy. *Amer. Surg.* 26:219, 1960.
32. Sabiston, D. C., Jr., Fauteux, J. P., and Blalock, A.: An experimental study of the fate of arterial implants in the left ventricular myocardium. With a comparison of similar implants in other organs. *Ann. Surg.* 145:927, 1957.
33. Schildt, P., Stanton, E., and Beck, C. S.: Communications between the coronary arteries produced by application of inflammatory agents to the surface of the heart. *Ann. Surg.* 118:34, 1943.
34. Sewell, W. H.: Results of 122 mammary pedicle implantations for angina pectoris. *Ann. Thorac. Surg.* 2:17, 1966.
35. Sewell, W. H.: Coronary arteriography, nitrates and implant operations in the management of coronary artery disease. Address to Yale University School of Medicine. February 25, 1969.
36. Sewell, W. H., and Sealy, W. C.: Coronary cinearteriography and pedicle operation in diagnosis and treatment of coronary insufficiency. *Surgery.* 55:99, 1964.
37. Sones, F. M.: *Cinecardioangiography: Clinical Cardiopulmonary Physiology.* New York: Grune & Stratton, 1960.
38. Stanton, E. J., Schildt, P., and Beck, C. S.: The effect of abrasion on the surface of the heart upon intercoronary communications. *Amer. Heart J.* 22:529, 1941.
39. *Statistical Abstract of the United States 1966.* Washington: Government Printing Office, 1966.
40. Thompson, S. A., and Raisbeck, M. J.: Cardiopericardioplexy. *Ann. Intern. Med.* 16:495, 1942.
41. Urschel, H. C., Jr., and Morales, A.: Posterior myocardial revascularization by retrograde internal mammary artery implantation. Presented at the 20th annual meeting of The Society for Vascular Surgery, Chicago, Ill., June 26, 1966.
42. Vineberg, A.: Development of anastomoses between the coronary vessels and a transplanted internal mammary artery. *Canad. Med. Ass. J.* 55:117, 1946.
43. Vineberg, A., Deliyannis, T., and Pablo, G.: Myocardial nutrition after the Ivalon sponge operation, the return of a four-hundred million year old system. *Canad. Med. Ass. J.* 80:948, 1959.
44. Vineberg, A., Shanks, J., Pifarre, R., Criollos, R., and Kato, Y.: Combined internal mammary artery implantation and free omental graft operation: A highly effective revascularization procedure. *Canad. Med. Ass. J.* 90:717, 1964.
45. Vineberg, A., and Walker, J.: The surgical treatment of coronary artery heart disease by internal mammary artery implantation: Report of 140 cases followed up to 13 years. *Dis. Chest.* 45:190, 1964.
46. Wearn, J. T., Mettler, S. R., Clumpp, T. G., and Zschiesche, L.: The nature of vascular communications between the coronary arteries and the chambers of the heart. *Amer. Heart J.* 9:143, 1933.

Scintillation Scanning in a Community Hospital A Review: Part II

Chester J. Kay, M.D.

Lung

Lung scanning provides a safe, simple method of estimating regional pulmonary arterial perfusion.¹ It detects areas of ischemia far more efficiently than the conventional chest roentgenogram and consequently has its most important application in the early diagnosis of pulmonary embolus. It serves as an excellent screening test for those patients who may require pulmonary angiography.

When radioiodinated particles of macroaggregated albumin, over 10 microns in size are injected intravenously, they are efficiently trapped in the vascular bed of the lung. Although they temporarily block these arterioles or capillaries, the number of vessels involved is so small compared to the number present, that no change in pulmonary hemodynamics is produced.² The half-time of the macroaggregates in the lung is four to eight hours. They are broken down into smaller particles and are phagocytized and metabolized in the reticuloendothelial cells of the liver and spleen. Extensive testing for toxicity has thus far shown that the material is safe at the recommended dosage levels even in patients with severely impaired cardiopulmonary function.

The thyroid gland should be blocked by doses of Lugol's solution before and after the scan. The injection of 200 to 300 microcuries of macroaggregated albumin is made slowly with the patient breathing deeply and preferably by drawing back only a minimal quantity of blood into the syringe. Posture influences the distribution of the particles.³ We usually inject with the patient supine. Injection in the erect position may be made when the basilar areas are of special interest. The patient is immediately scanned in the anterior and posterior projections. Lateral scanning may be helpful and may be the only diagnostic view when right middle lobe

pathology is present.⁴ The normal scan is shown in Figure 1. When pulmonary emboli are present, one



Figure 1
Normal posterior perfusion lung scan.

or more areas of decreased activity are seen (Fig. 2). The site and extent of arterial obstruction may be appreciated from the scan. More than one region of the lung is involved in 65% of emboli.⁵ If the embolus does not go on to infarction, a companion chest x-ray will not show an infiltrate. The combination of a perfusion defect and a "normal" chest radiograph is very suggestive of a pulmonary embolus. In the presence of an infiltrate on the chest radiograph, the scan is more difficult to evaluate since pneumonia, abscess, atelectasis, neoplasm and sequestration, as well as pleural effusion, pleural thickening, blebs, bullae and other entities all may produce defects on the scan. The presence of multiple defects on the scan, as well as serial scans, may be helpful in these cases. Angiography may be necessary. Cardiomegaly may produce an area of decreased perfusion in the left lower lung field. Acute asthma can produce multiple defects in ar-

DR. CHESTER KAY, attending radiologist at Park City Hospital, Bridgeport, and clinical instructor in radiology at the Albert Einstein College of Medicine.



Figure 2

Bilateral pulmonary emboli, as shown by a posterior lung scan.

terial perfusion and with a normal chest radiograph, can mimic the scan findings of emboli exactly⁶ (Fig. 3). A clinical history is necessary for proper interpretation.

The perfusion scan has been used to evaluate the extent of lung neoplasms by the ischemia produced from compression of the pulmonary artery by the primary tumor or nodes. The scan offers an excellent test of regional pulmonary function.⁸ It has also been used to evaluate regional changes in pulmonary hemodynamics such as in mitral stenosis.⁹

When the scan is suggestive of emboli, and surgery either in the form of pulmonary embolectomy or inferior vena cava plication or ligation is going



Figure 3

Lung scan during an acute asthmatic attack. Note bilateral perfusion defects.

to be performed, pulmonary angiography should be done to document the lesion and its extent. Small, peripheral emboli may be seen on the scan and not be appreciated by angiography. Even smaller peripheral emboli may be missed by both these diagnostic entities.

The combination liver-lung scan may be valuable in diagnosing some cases of subphrenic abscesses.¹⁰

Both indium^{113m} and technetium ^{99m} labeled macroaggregated albumin are being evaluated as new radiopharmaceuticals for perfusion lung scanning.

Inhalation scanning is used to assess airway patency both proximally and distally. The radio-aerosol inhalation lung scan is performed by having the patient inhale any one of several radionuclides in the form of fine particles through a closed system such as the Bird respirator.¹¹ The normal scan shows nearly uniform distribution of radioactivity throughout the lung, indicating patency of the bronchi. In the presence of complete bronchial obstruction, no radioactivity is noted distal to the block. In incomplete obstruction, there is increased activity at the site of obstruction with reduced deposition of the isotope distally. The inhalation scan is thus an adjunct to bronchography in the assessment of airway patency. Though very valuable in certain individual cases, its ultimate place in the clinical armamentarium is still being evaluated.

Kidney Scanning

The agents currently available for renal scanning localize in the renal parenchyma, principally in the cortex. The most widely used agent, mercury 197-chlormerodrin is concentrated in the tubular cells of the kidney. The usual dose for a scan in adults is 100 to 125 microcuries. This delivers 0.5 to 1 rad to the kidney and 2 to 8 millirads to the whole body. The patient is scanned one hour after the intravenous injection.

Since its introduction, renal scanning has gained wide acceptance. The normal scan (Fig. 4) shows homogenous activity throughout the kidney except near the hilum where it is slightly diminished. The margins may be somewhat blurred due to respiratory motion. Minimal hepatic activity is normally present.

Focal lesions interfering with tubular function appear as cold areas. Thus, space occupying disease such as a cyst, tumor, or abscess would show decreased activity (Fig. 5), whereas fetal lobulation would have normal activity. Lesions smaller than 2 to 3 centimeters will usually be missed unless located peripherally. The differentiation of a benign



Figure 4
Normal Hg¹⁹⁷ chlormerodrin renal scan.

from a malignant lesion cannot be made by the conventional scan. However, the technetium^{99m} pertechnetate blood flow study with a gamma-ray scintillation camera, may show a tumor "blush" in some cases of cancer.¹² There are false positives and false negatives and the overall accuracy of this intravenous technique appears to be below that of selective renal arteriography.

Renal scanning provides a gross evaluation of renal function. For example, in cases of long standing hydronephrosis due to ureteral obstruction, the demonstration of significant residual functioning renal parenchyma on the scan may enable the patient to have a conservative procedure rather than nephrectomy. Neither intravenous urography nor angiography provide this information as well.

In renal insufficiency, the kidneys do not handle the chlormerodrin adequately but the scan can be performed in the usual manner with blood urea

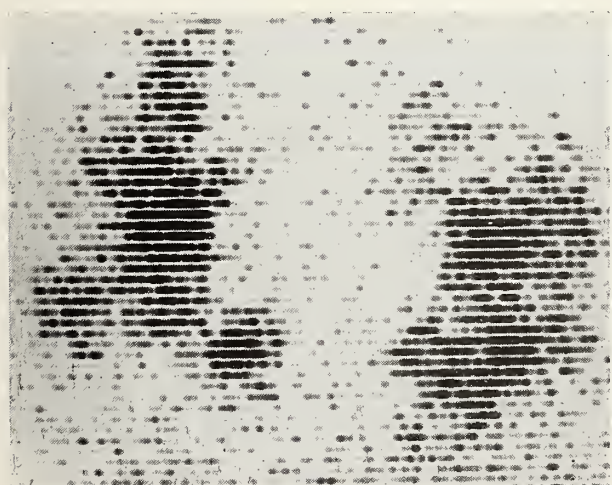


Figure 5

Polycystic disease of the kidneys. Note enlarged kidneys bilaterally filled with multiple defects.

nitrogen levels up to 60-80 mg%. High body background and increased hepatic pickup is noted on the scan. The latter may overlie the right kidney and make scan interpretation confusing. A delayed scan may be helpful in those patients with higher levels. In patients with renal failure, scanning with I-131 labeled hippuran is the agent of choice since the material is retained in the kidneys long enough to scan them.¹³ Renal size and the amount of functioning parenchyma may be evaluated.

The scan has generally been considered a valuable adjunct to intravenous urography in screening patients for renovascular hypertension. To some, it has been disappointing. The I-131 hippuran renogram is considered preferable, but if not available, the Hg¹⁹⁷ chlormerodrin scan and renogram¹⁴ should be performed in addition to a urogram as a preliminary screening procedure. Evidence of infarction on the scan, or decreased size or activity in one kidney with the latter not explained by a morphologic abnormality on the urogram, are findings associated with renovascular hypertension. Unilateral or bilateral decreased activity may be associated with inflammatory disease or any one of many entities interfering with tubular function.

The scan has been very helpful in cases of renal trauma.¹⁵ Specific patterns may be discerned in renal rupture, infarction and contusion. Correlation with angiography is excellent.

Inadequate intravenous urograms, allergy to organic iodides, documentation of congenital abnormalities such as ectopic or horseshoe kidneys, and location of the kidney for renal biopsy are other indications for renal scanning.

Dynamic studies with I-131 hippuran or technetium^{99m} pertechnetate utilizing the scintillation camera should extend the diagnostic scope of renal scanning in the coming years. A technetium^{99m} iron complex is currently being evaluated as a new scanning agent.

Placental Scanning

Accurate localization of the placenta can be of prime importance in the management of antepartal hemorrhage. Localization of the placenta is also helpful in abdominal pregnancy, intrauterine fetal transfusion and amniocentesis. Conventional radiographic techniques can be used. However, isotope placentography¹⁶ greatly improves the accuracy. Scanning with technetium^{99m} labeled serum albumin or radioiodinated serum albumin provides a direct picture of the placenta and its relationship to the pubis.¹⁷ Preliminary data have shown good

accuracy¹⁸ in diagnosing placenta previa although the results with a large series of patients including the false positive rate have not been published.

Acknowledgment

Appreciation to Mrs. Mary Stephenson without whom this series of papers could not have been done.

Bibliography

1. Quinn, J. L., III and Wheatley, J. E., Lung Scintiscanning, *Radiology*, 83-937, 1964.
2. Gold, W. M. and McCormack, K. R., Pulmonary function response to radioisotope scanning of the lungs, *J.A.M.A.* 197: 146, 1966.
3. Poe, N. D., Swanson, L. A., and Taplin, G. V., Physiologic factors affecting lung scan interpretations, *Radiology*, 89: 661, 1967.
4. Suprenant, E. L., Lateral Lung Scanning: Anatomic and Physiologic considerations, *Am. J. Roentgenol.*, 99: 533, 1967.
5. Tow, D. E., and Wagner, H. N. Jr., Recovery of arterial blood flow in patients with pulmonary embolism, *New Eng. J. Med.*, 276: 1053, 1967.
6. Mishkin, F., and Wagner, H. N. Jr., Regional abnormalities in pulmonary arterial blood flow during acute asthmatic attacks, *Radiology* 88: 142, 1967.
7. Maxfield, W. S., Hatch, H. B., Jr., and Ochsner, J. L., Perfusion Lung Scanning in evaluation of patients with bronchogenic carcinoma, *Surg. Clin., N.A.*, 46: 1389, 1966.
8. Tow, D. E., Wagner, H. N. Jr., Lopez-Majano, V., Smith, E. M. and Migite, T., Validity of measuring regional pulmonary arterial blood flow with macroaggregates of human serum albumin, *Am. J. Roentgenol.*, 96: 664, 1966.
9. Friedman, W. F., and Braunwald, E., Alterations in regional pulmonary blood flow in mitral valve disease studied by radioisotope scanning, *Circulation*, 34: 363, 1966.
10. Brown, D. W., Lung-liver radioisotope scans in the diagnosis of subdiaphragmatic abscess, *J.A.M.A.*, 197: 728, 1966.
11. Taplin, G. V., Poe, N. D., and Greenberg, A., Lung scanning following radioaerosol inhalation, *J. Nuc. Med.*, 7-77, 1966.
12. Rosenthal, L., Radionuclide diagnosis of malignant tumors of the kidney, *Am. J. Roentgenol.*, 101: 662, 1967.
13. Rosenthal, L., Orthoidohippurate-¹³¹I Kidney scanning in renal failure, *Radiology*, 87: 298, 1966.
14. Meier, D. A., Beierwaltes, W. H., Radioisotope renal studies and renal hypertension. A comparison of the sodium iodohippurate ¹³¹I renogram, Chloromerodrin Hg¹⁹⁷ uptake and renal scan, *J.A.M.A.*, 198: 1257, 1966.
15. Freeman, L. M., Kay, C. J., and Meng, C., The contribution of renal scanning in the evaluation of renal trauma, *Radiology*, 86: 1021, 1966.
16. Schreiber, M., and Red, D. E., Placentography, *Radiol. Clin., North America*, 5: 47, 1967.
17. Nelp, W. B., and Larson, S. M., Diagnosis of placenta previa by photoscanning with albumin labelled with ^{90m}Tc., *J.A.M.A.*, 200: 148, 1967.
18. Johnson, P. M., Sciarra, J. J., O'Leary, J. A., Placental scanning with sodium pertechnetate ^{99m}Tc serum albumin, *Radiology*, 89: 321, 1967.

The Impact Of Science On Clinical Methods

When one considers the orgy of venesection indulged in during the many centuries of the past it is curious to observe, in the second half of the nineteenth century, a marked aversion to venepuncture for the purpose of obtaining blood for chemical analysis. This, no doubt, was due to the influence of the bacteriological discoveries of the time, and the fear of introducing infection. It was not due to the lack of a suitable instrument, for Pravaz, in 1851, and Wood, in 1855, had introduced the hypodermic syringe, but no one dared insert this into a vein until Wright began taking blood for blood culture, about 1900.

There were two results of this reluctance: one was a long period in which very little blood chemistry was done; the other was the development of micro-methods using capillary blood from finger-prick as introduced by Bang at the end of the century, by means of which he made estimations of chlorides, sugar, proteins, fats and cholesterol.

After 1900, taking blood by venepuncture gradually came into use, and after 1904, when Folin estimated creatine and creatinine in the urine colorimetrically, this method was extended to estimations of urea, uric acid, glucose and cholesterol in the blood. The substitution of the photoelectric cell for subjective matching of colours greatly enhanced the usefulness of all colorimetric methods, including that of flame photometry. This had been initiated by Bunsen and Kirchoff in 1860, and at that time they had seen its very wide potentialities for detecting traces of elements by spectrum analysis. . . .—Keele, K.D.: *The Evolution of Clinical Methods in Medicine*, Charles C. Thomas, Publisher, 1963, p 73.

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THE PRESIDENT'S PAGE

Soaring Medical Costs

During the past decade, the increasing cost of delivery of medical care has plagued the practice of medicine with alarming intensity. While a variety of factors may be cited to account for such costs such as general inflation, "fantastic" increase in demand for medical services, Federal health programs, "medicine's" success in developing techniques and equipment and health education of the public, probably the two most outstanding pressures are (1) increasing hospital costs and (2) physicians' fees. It is gratifying to note, although belatedly, that following Congressional investigations, labor union's furor and recent unfavorable news media publicity, the American Hospital Association and the American Medical Association, have become concerned with programs to control 'soaring medical costs' and still provide optimum care to all patients. The question is: just what mechanisms can be used by both associations?

In a recent periodical, the American Hospital Association predicted a change from a "concentration of beds with outpatient facilities attached" to an "ambulatory care center with inpatient beds attached." This prediction was based on a conference report which contained guidelines for planning, establishment or re-organization of hospital outpatient departments. It was also reported that in the past 15 years, outpatient usage of hospitals increased at double the rate of inpatient use. It is significant to note that the AHA report states that "the care of the hospital may remain intensive patient care" but that the chief major function to the community should be ambulatory care. The latter includes multiphasic screening, preventive services, diagnostic and treatment services, home care programs, health related social services and a network of relationships with other health care programs. Recently, the Chairman of the Committee on Hospitals of the Connecticut State Medical Society reported on the 51st Annual Meeting of the Connecticut Hospital Association. She emphasized that two programs have been recently launched to help control the spiraling costs of hospital care, i.e., The Pilot Study on Incentive Reimbursement and a recently inaugurated systems engineering program. Emphasis was also put on other expanded programs, i.e. manpower recruiting and training, establishment of operational standards for hospitals, cost containment programs, provision for shared services whenever possible and closer liaison with other professional groups, health agencies, and planning boards.

The significant and timely question is "What is the medical profession doing to stem spiraling medical costs.—Suggestions from the AMA, state medical societies and county associations have been made, the most important of which may be enumerated as follows:

1. *Decreased Hospitalization*

Physicians should hospitalize patients only when necessary. A careful screening of patients, and the laboratory work ordered for them, etc. should be done in the physicians office, or Emergency Room. Orders should be issued only for necessary tests. Without question, decreased hospitalization is a significant single factor in helping to cut total medical expenditures in this state and this country. This has been emphasized by not only the medical profession and the American Hospital Association but also by others concerned in the delivery of medical care.

2. *Decrease in Orders For Laboratory Tests etc. When Patients Are Hospitalized*

All too often physicians have "routine orders" written out as an aid to nurses for their patients upon admission. Such routinization of orders should be replaced by "tailor making" prescribed orders to meet the immediate needs of the patient at any single admission to a hospital. Unwarranted full scale

laboratory procedures have added considerably to medical costs. If commercial laboratories are employed by a physician, charges for laboratory work should be made to the patient directly by the laboratory concerned. This would help eliminate "profiteering" by some referring physicians through mark-ups on commercial laboratory services.

3. *Decreased Hospital Stay Unless Warranted*

Fortunately the efforts of utilization committees in hospitals has cut down unwarranted, lengthy hospitalization. However, occasional instances still appear at state and county levels of unnecessary extensions of patient hospitalization. Education and self-discipline for physicians should eliminate this factor which adds to medical costs.

4. *Greater Emphasis On Ambulatory and Office Care For Diagnostics and Some Therapeutic Procedures*

The use of a physician's office or outpatient clinics would greatly decrease the unnecessary use of beds for ordinary diagnostic procedures and some simple therapeutic measures. Recommendation of the use of a physician's office for such procedures by insurance companies and other third party payors is certainly wise, appropriate and most urgent.

5. *Institute An Educational Program Not Only For All Physicians But The Public-At-Large Concerning Health Care*

This is one of the most important factors in helping to cut down medical costs. All too often patients feel they are not getting optimum medical care unless they are hospitalized. This is a "shibboleth of the patient." To emphasize again, patients should only be hospitalized when necessary for the delivery of optimum care. If the medical profession is not successful in controlling medical costs, someone else, perhaps the Government, will do it. We already know the effects of the intrusion of the Government in medical practice and the dismal failures resulting therefrom.

6. *Restructure Present Private Insurance Programs*

Private insurance programs for basic coverage do not now make provision on a large scale for outpatient care, either in the hospital or doctor's office. Future coverage may have to include recognition of where the greatest delivery of medical services are given—in the doctor's office. If this is done, there may be relief from the pressures doctors feel about hospitalizing patients to insure coverage of costs for the individual patient.

STEVENS J. MARTIN, M.D.



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In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.

Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.

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CALL

SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1969 Semi-Annual Meeting of the House of Delegates will be held at the New Haven Medical Association Building, 364 Whitney Avenue, New Haven, commencing at 2:00 o'clock in the afternoon of Thursday, December 11.

Stevens J. Martin, President
Kenneth F. Brandon, Speaker of the House
Reginald C. Edson, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12 Par. 3 of the By-laws provide that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the By-laws were introduced at the House of Delegates on May 14, 1969 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendments shall be taken off the table and acted upon by the House of Delegates."

I. Vice-Chairman of the Council

Purpose: To establish the office of Vice-Chairman of the Council and define the duties thereof.

AMENDMENT

Article VII—The Council

Section 1. Powers and Duties

Paragraph 2. Chairman—Delete the entire paragraph and substitute the following.

Paragraph 2. Chairman and Vice Chairman. The Council shall annually elect from its membership a Chairman and Vice-Chairman.

The Chairman shall preside at all regular and special meetings of the Council and shall perform such duties as custom and parliamentary usage require. He may address the Council at the opening of any meeting of the Council, limiting his remarks to matters of conduct and procedure in the Council. He shall have full voting rights in the Council.

The Vice-Chairman shall aid and assist the Chairman and shall officiate for the Chairman during his absence or at his request. In the case of death, resignation or removal of the Chairman, the Vice-Chairman shall immediately become Chairman and shall serve the remainder of the term of his immediate predecessor. He shall have full voting rights in the Council.

In the absence of both the Chairman and Vice-Chairman, the President shall preside.

II. The Judicial Committee

Purpose: To make it mandatory for the Judicial Committee to file a report at each annual meeting of the House of Delegates.

AMENDMENT

(Add the underlined words)

Article X. Committees of the Council

Section 3. Judicial Committee

Paragraph c. (5) The Judicial Committee shall render a semi-annual report to the Council including its actions, opinions, and recommendations and shall make such interim reports as it desires or as are requested by the Council. Such reports shall be available to members of CSMS.

The Committee shall also file a report of its activities at each annual meeting of the House of Delegates.

III. The Judicial Committee

Purpose: To require the endorsement of the House of Delegates on any "rule of ethics" recommended by the Judicial Committee before it becomes binding upon all members of the Society.

AMENDMENT

(Add the underlined words)

Article X. Committees of the Council

Section 3. Judicial Committee

Paragraph c(1) . . . Its (the Judicial Committee's) decisions shall be binding on the parties concerned and specific problem considered, but shall be considered only as a presumption of the Society, binding on all members only when endorsed by the Council and the House of Delegates and published by the Society to the membership.

IV. Committee on Medical Care of Veterans

Purpose: To abolish the Committee on Medical Care of Veterans and transfer its duties to the Committee on Third Party Payments.

AMENDMENT

Article XI. Divisional Boards and Committees

Section 3. Divisional Standing Committees

Paragraph c. Medical Economics Division
Delete the words "Committee on Medical Care of Veterans"

Section 5. Duties of Standing Committee

Paragraph 10. Committee on Medical Care of Veterans. (Delete in its entirety.) Renumber paragraphs 10 through 28

Paragraph 12. Committee on Third Party Payments. (Delete underlined words.) . . . In its opera-

tions, the committee shall confer directly with agencies which have an interest and responsibility in systems that involve payment of physicians by third party agencies but, where other standing committees of The Society have direct relationships, such as the Committee on Medical Care of Veterans, the committee shall confer with such other standing committees rather than directly with the agencies involved.

V. Committee on State Blood Bank

Purpose: To expand the duties of the Committee on State Blood Bank to include organ transplants.

AMENDMENT

Article XI. Divisional Boards and Committees

Section 3. Divisional Standing Committees

Paragraph (F) Scientific Activities Division
(Change name of Committee to read:)
Committee on Organ and Tissue Transfers

Section 5. Duties of Standing Committees

Paragraph 20. (Add following sentence)

The Committee shall also keep abreast of developments in the field of organ and tissue transfers and the procurement, processing and preservation of organs and tissues used in such transfers and shall cooperate with other interested agencies in the establishment and maintaining of high professional standards in the subject areas.

Placement Wanted

INTERNIST—34 years of age, Board certified with National Boards desires group or associate practice in Connecticut. Military obligations completed. Available immediately. Interest in practicing general Internal Medicine.

ORTHOPEDECS—37 years of age, Board certified with National Boards desires partnership in Connecticut. Military obligations completed, available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

Placement Opportunities

SENIOR STAFF PSYCHIATRIST, full time, residential psychiatric rehabilitation center 40 miles from New York City, in desirable living area with good schools. Non-profit Foundation oriented to intensive, individualized, eclectic psychotherapy. Large out-patient service. Salary open, dependent on experience. Benefits include major medical insurance, life insurance and pension program. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

PHYSICIAN, to cover every other weekend and certain holidays, a well organized general practice consisting mostly of adults, and no one under the age of ten. Salary is \$1300.00 a year plus the fees collected.

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GENERAL PRACTITIONER, for additional Senior Physician at the Connecticut State Prison. Opportunity exists for part time outside practice if desired, in nice community. Salary range \$16,370.00 to \$19,970.00. Three weeks vacation, plus sick leave, eleven paid holidays, three annual earned leave days, time off for medical meetings. Excellent health insurance. Contact Mr. Parson, Personnel Department, Connecticut State Prison, Somers, Connecticut 06071.

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CHIEF OF MEDICINE—At accredited State Veterans general medical and surgical hospital of 496 beds, with a domiciliary section of 800 beds. Hartford area. Duties: Directs the facility's program in

medicine; related work as required. Age limit: Up to 65 years, if in good health. Experience and training: Completion of general internship in AMA-approved hospital, and not less than 5 years employment with emphasis in the field of medicine and/or certain equivalent qualifications to be evaluated individually. Salary range—Open. For further information and application forms, write to: Frank Mongillo, M.D., Chairman, Veterans Home and Hospital Commission, Rocky Hill, Connecticut.

GENERALISTS, INTERNISTS AND PEDIATRICIANS—Northern Connecticut city of 47,000 in need of 2 General Practitioners, 2 Internists and 1 Pediatrician. Can readily be assimilated into physician community over next 3 years. Hospital privileges available; also good office space available near hospital. Those interested in establishing solo practice in the fields named may obtain further information from: Martin Duke, M.D., Director of Medical Education, Manchester Memorial Hospital, Manchester, Connecticut 06040.

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Scientific Section Membership Urged For CSMS Members

The Bylaws of the Connecticut State Medical Society (Article VIII, Section 2, Paragraph 2) provide for the formation and operation of scientific Sections as follows:

PAR. 2. SECTIONS

- (A) **PURPOSES:** To conduct the work of the Scientific Assembly and for related purposes, the formation of Sections of the Society may be authorized by the House of Delegates.
- (B) **AUTHORIZATION:** Sections of the Scientific Assembly may be created or discontinued by the House of Delegates in accordance with Article V, Section 1 of these Bylaws. Any group of physician members of the Society having a common interest in a recognized branch of medicine may, through application filed with the Council, petition the House of Delegates for authorization to form a Section in that recognized branch of medicine.
- (C) **PETITION:** A petition to the House of Delegates for authorization to form a Section shall be submitted first to the Council. It shall be in writing and include a roster of interested members, officers pro tem, and a set of bylaws which contain the purposes of the Section and the provisions for granting membership, assessment of dues and the election of officers. Such petition shall be examined by the Council and, if found to be in order, shall be transmitted to the next regular meeting of the House of Delegates with recommendation.
- (D) **MEMBERSHIP:** It is the intention of the House of Delegates that the sole qualifications for physician membership in a Section of the Scientific Assembly shall be (1) Active or Life Membership in good standing in the Society, and (2) a bona fide, demonstrable interest in the work of the Section; and that there shall not be other contingent qualifications for such membership. Questions concerning these qualifications shall be resolved by the Council.
- (E) **OFFICERS:** Each Section shall have, as officers, a chairman and a secretary and such other officers as the members of the Section may deem advisable, each to be elected by the voting members of the Section during the annual meeting of the Scientific Assembly and to serve for one year. The rights to vote and hold office in a Section shall be limited to physician members of the Society who are in good standing.
- (F) **MEETINGS:** Each section shall hold a meeting during the course of the annual meeting of the Scientific Assembly and at such other times as the members or officers may deem advisable. The officers of each Section shall arrange the programs for the annual meeting during the Scientific Assembly in accordance with rules established by the Council and the House of Delegates.

All members of the Society, and especially those currently being admitted to membership, are encouraged and urged to join the Section that is concerned with the area of medical practice in which the member engages and/or in which he has a "bona fide interest". The advantages of Section membership are several and meaningful. Some of these are: First, the physician identifies himself with a professional peer group within the Society. Second, he is eligible to participate in the deliberations of his Section, not only those of a purely scientific nature but those of a socio-economic nature as well. Through this mechanism, the member has an equal "voice" with his fellows throughout the state on matters of common interest and concern to practitioners in his field and to the Connecticut profession generally. Third, he has opportunity to serve as the representative and spokesman for his colleagues; i.e., as a Section officer, a committee member, on the Executive Committee, in legislation, etc. Such service is rewarding in that it requires that he keep abreast of important developments in his own and related fields of medical practice and maintain an awareness of the views and interests of the Section membership.

At the present time, there are extant 22 Sections within the Society, most of which are active and serving a useful purpose. They are listed herewith:

Section on Allergy	Section on Ophthalmology
Section on Anesthesia	Section on Orthopedic
Section on Aviation Medicine	Section on Otorhinolaryngology
Section on Dermatology and Syphilology	Connecticut Society of Pathologists
Section on Gastroenterology	Section on Pediatrics
Section on General Practice	Section on Physical Medicine
Section on Internal Medicine	Section on Preventive Medicine and Public Health
Section on Neurology	Section on Proctology
Section on Neurosurgery	Connecticut District Branch of the American Psychiatric Association
Section on Obstetrics and Gynecology	Section on Radiology
Section on Occupational Health	Section on Urology

For emphasis, it is repeated that each CSMS member is encouraged and urged to join the Section that is concerned with his area of practice and/or in the work of which he has a bona fide interest. By so doing, he will benefit personally from his participation and will assist the Society in carrying out its functions "to extend medical knowledge and advance medical science; to elevate the standards of medical education; to promote friendly intercourse among physicians; and to enlighten and direct public opinion so that the profession shall become increasingly useful to the public in the prevention and care of disease and in prolonging and adding comfort to life."

Information regarding application for Section membership may be obtained from the Executive Director's Office, Connecticut State Medical Society, 160 St. Ronan Street, New Haven, Connecticut 06511.

A BREATH OF FRESH AIR

In these times when so many of the loudly vocal critics of our profession are contending that today's medical men are almost universally cold, impersonal and disinterested in their attitude toward patients, it is a real pleasure to publish (anonymously) a letter recently received by the President of the Society. So far as is known, the physician member about whom it is written is not necessarily aware of the high esteem in which he is held by an entire family group. The letter follows:

Dear Doctor Martin,

Dr. ————, of ————, has been our family doctor for over five years. In this period he has taken time, and had the patience, to give our family the best of care and has, I am sure, kept us from the more serious consequences of illnesses by his preventive medical techniques. There is a great deal that could be said of his physician's skill.

However, I must mention him as a fine person—above and beyond his medical abilities. With us, he has shown that he is truly interested in us as a family group, and has treated us in a personal manner that goes far beyond his responsibilities to us as a doctor.

In today's very busy society, it is the kindly acts of Doctor ———— which make us stop and realize that we are not just a cumulative record in the doctor's office. (He) has the capacity to make one feel important even at his busiest times.

It is really difficult to explain how we feel about this man, except to say that he is "Mr. Doctor" plus, plus and plus.

Very truly yours,
——— and family

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by

HYMAN M. CHERNOFF, M.D.

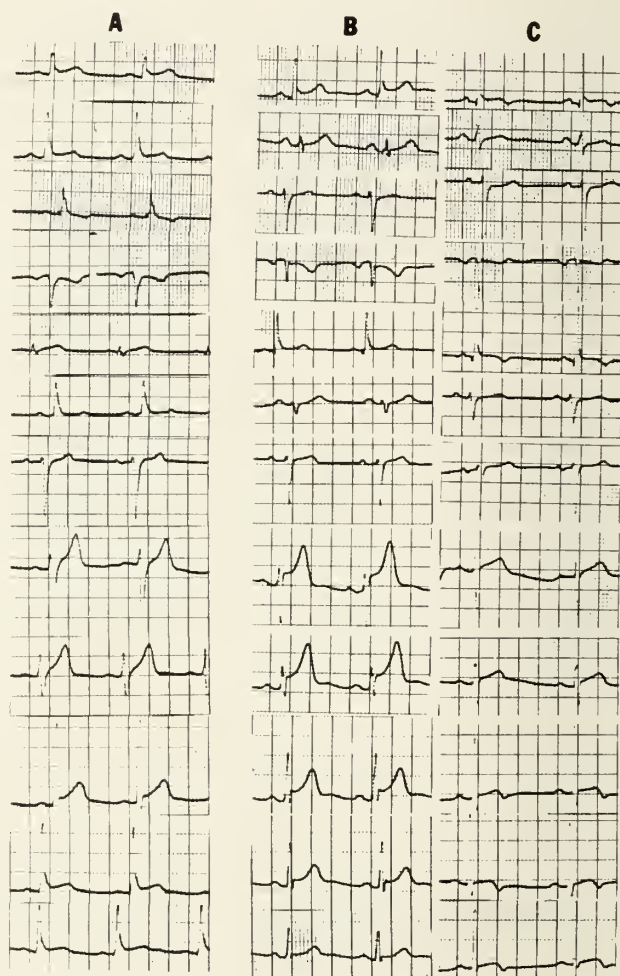
Associate Professor of Clinical Medicine,
Yale School of Medicine

Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Normal electrocardiographic variants often simulate the patterns associated with the presence of heart disease. Unless the clinical setting is carefully examined, reliance on the tracing alone may lead to false diagnosis and even inappropriate therapy. Above are the electrocardiograms of two different patients. Tracing A was obtained during the routine workup of a 36 year old black male admitted to the Yale New Haven Hospital because of epigastric pain attributed to the known presence of a duodenal ulcer. There was no complaint of chest pain and no pericardial friction rub was heard. The electrocardiogram reveals concave elevation of the ST segments in leads 1, 2, aVF, V4, V5, and V6. These changes in this clinical setting were considered to represent the normal ST variant rather than evidence of acute pericarditis. This ST variant is commonly seen in the young black male in the absence of any evidence of myocardial or pericardial disease. It may also be occasionally seen in whites. Serial tracings in our black patient failed to reveal any progressive change in the configuration of the ST segments and no evidence of clinical pericarditis developed.

Tracings B and C belong to a 64 year old white male who was admitted to Yale New Haven Hospital on 11-5-64 with a diagnosis of lobar pneumonia. Tracing B, obtained on the day of admission, revealed concave ST elevation in leads 1, aVL, V2, V3, V4, V5, and V6, changes similar to those present in the tracing obtained in the young black male with the duodenal ulcer. In this clinical setting, however, these ST changes were considered to be consistent with the presence of acute pericarditis. On the second hospital day a pericardial friction rub was first heard. Tracing C, taken on the 7th hospital day, revealed subsiding of the concave ST elevations and terminal inversion of the T-waves in

leads 1, aVL, V4, V5, and V6, changes typical of the evolution of the pericarditis pattern.



The normal ST variant is believed to result from accelerated ventricular repolarization. Its gross similarity to the injury potential resulting from acute pericarditis is well illustrated above. The clinical picture and serial electrocardiograms are helpful in excluding the presence of acute pericarditis.

Letters To The Editor

Members of the Society are invited to communicate with the Editor expressing their opinions or giving information as to any matter of interest to the members. The Editorial Board reserves to itself the right to select the communications or excerpts therefrom that will be published and to reject others. As with other material which is submitted for publication, all letters will be subject to the usual editing. Address all correspondence to: THE EDITOR, CONNECTICUT MEDICINE, 160 St. Ronan Street, New Haven, Connecticut 06511.

Dear Dr. Nahum:

The case presented by Dr. Pochedly and Dr. Ente in the August, 1969 issue is of considerable interest. I question, however, whether the documentation of disseminated intravascular coagulation is sufficient to justify the diagnosis. The laboratory support for this diagnosis consists of an elevated Partial Thromboplastin Time and decreased Fibrinogen level. Since the Prothombin Time was normal and the abnormal PTT was not corrected by the addition of factors VIII, IX or XI, the assumption is implicit that there were no factor deficiencies present. The diagnosis of a defibrination syndrome without evidence of factor deficiencies or of depressed platelet levels is questionable. Perhaps, if factor assays had been performed, a deficiency of at least factors V and VIII might have been demonstrated, thus strengthening the diagnosis. I would not attach too much significance to the poor clot retraction in that this may have been partially related to the polycythemia.

Since the laboratory diagnosis of disseminated intravascular coagulation is a difficult one to establish, it is a difficult diagnosis to exclude. Certainly, the low fibrinogen level and elevated PTT have to be explained. Most of my objections to a diagnosis of defibrination would also extend to a diagnosis of primary fibrinolysis, certainly a more rare clinical event. I wonder if a circulating anticoagulant might not have been implicated, particularly in view of the failure of added clotting factors to correct the PTT.

Sincerely yours,
Paul Bachner, M.D.

Associate Attending Pathologist
The Greenwich Hospital Association
Greenwich, Connecticut

Dear Dr. Bachner:

Thank you for your interest and comments on our article. You are correct in saying that the coagulation work up of our baby was incomplete. I am chagrined that plasma was not frozen and studied at one of the excellent coagulation laboratories in New York.

We have since encountered instances of disseminated intravascular coagulation in children with fulminating infectious mononucleosis, glomerulonephritis and Rocky Mountain Spotted Fever. A variety of coagulation factor deficiencies have been observed, mainly factor II, factor V, factor VIII, and factor X.

Dr. Arturo Aballi reviewed the MSS and his comments are enclosed. Your criticisms are well taken and we are grateful for your interest.

With kindest regards.

Sincerely yours,
Carl Pochedly, M.D.

Director, Pediatric Hematology
Meadowbrook Hospital
East Meadow, N.Y. 11554

Dear Dr. Pochedly:

I have reviewed your interesting MSS. It is clear that your patient had an excellent work up and illustrates very well the circulatory embarrassment which may occur in the course of *hyperviscosity*, particularly when associated with a markedly increased blood volume. We have seen a few patients with prolonged intrauterine hypoxia which had a polycythemia with a marked increase in immature erythrocytes. In other similar cases (like in your own) it was not possible to document the prolonged intrauterine hypoxia.

Unquestionably a patient with Down's syndrome is predisposed to other alterations of hematopoiesis. The presence of giant platelets is interesting. We have seen them often in very small prematures, but not in full term babies.

It is quite probable that, as you point out, this patient had some intravascular coagulation. However it is my feeling that the evidences in favor of intravascular coagulation (IVC) that you are offering are not too convincing. In our studies of *normal* newborns we have found some babies with fibrinogen levels below 150mg. In prematures such a

finding may be observed in about 10% of cases. The alteration of the PTT is even less significant. After the first 2 or 3 days we have frequently encountered prolongations of this test by 15-20 seconds in babies who were absolutely normal. Also 10% of infants with normal prothrombin times had alterations of such degree. The abnormality of clot retraction is not very rare in polycythemic blood.

We do believe that IVC may be of importance in the neonatal period and we have sent an *abstract* showing evidences in this direction. However those cases showed much more severe defects of the clotting mechanism.

I thank you for the opportunity to go over your MSS.

Sincerely yours,
Arturo J. Aballi, M.D.

Director of Pediatrics
Long Island Jewish Hospital
Jamaica, N.Y. 11432

MEETINGS

GENERAL

September 24 5:00 P.M.
177th Semi-Annual Meeting of the
Hartford County Medical Association
Hartford Hilton Hotel, Hartford
Speaker: Victor R. Fuchs, Vice President in Charge
of Research, National Bureau of Economic Research.
Subject, "The Economists Rx for the Medical Care Industry."

October 1
177th Semi-Annual Meeting of the
Fairfield County Medical Association
Greenwich Country Club
October 23
186th Semi-Annual Meeting,
New Haven County Medical Association
Waverly Inn, Cheshire
Business Meeting 3:00 P.M.; Social Hour and
Dinner to follow

November 4-6
26th Annual New England Postgraduate Assembly
Statler Hilton Hotel, Boston
Subjects include: Management of Diarrhea, Drug
Abuse and Drug Addiction, Differential Diagno-

sis of Anemia, Coronary Care and Remote Monitoring in the Community, Drug Therapy in Cardiovascular Diseases, Behavior Problems in the Young, and Peer Review. Luncheon speakers will discuss Medical Needs in the Coming Decade, Family Planning and Family Health, Problem-Oriented Medical Record.

Sponsored by the Council of the New England State Medical Societies. Program is acceptable for 21 prescribed hours by the A.A.G.P. Registration fee \$25. Contact Mr. Getty Page, 128 Merchants Row, Rutland, Vt.

MEDICINE

Peter Bent Brigham Postgraduate Medical Series
The series is aimed at the practicing physician, held the second Friday of each month September-May. Attendance limited to 100. Fee is \$30 per course or \$250 per series, lunch included.
Contact David P. Lauler, M.D., Peter Bent Brigham Hospital, Boston, Mass.

September 26-27
Regional Meeting (New England, Canada) of the American College of Physicians
Mary S. Harkness Auditorium, Yale Medical School

SURGERY

September 8-November 22
12th Series of Ophthalmology Postgraduate Courses
Postgraduate Institute of New York Eye and Ear Infirmary, 310 East 14th Street, New York City
At the conclusion of the regular series, there will be a one week postgraduate course designed as a review in basic sciences in ophthalmology. Write Jane Stark, Registrar, at the Institute.

January 15, 1970
Conference, Connecticut Chapter of the American College of Surgeons
Park Plaza Hotel, New Haven
Contact: Francis M. Hall, M.D.,
140 Woodland Street, Hartford

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Heroin And Public Health

Hans H. Neumann, M.D.

Hard-drug addiction in New Haven (and possibly in other major cities of Connecticut) has eclipsed by far tuberculosis as a public health problem. This refers to both morbidity and mortality, apart from the enormous social and economic impact on the community.

The programs, at present, emphasize education in an effort to prevent, and treatment in an effort to rehabilitate. There is little cause for satisfaction with either.

Education of adolescents regarding narcotics is necessary to some degree, but there is no evidence as to its effectiveness. If wrongly done or overdone, with an immature age group given to daring and defiance, it may have the paradoxical effect of promoting, if not glorifying, drug abuse. There are reports that educational films shown in schools in areas without drug problems have been followed by waves of glue-sniffing, previously unknown. Glue was obtainable, other drugs were not. It would appear that education should be brief and to the point, emphasizing the dangers without too many specific details of "how to".

Drug addiction has always been an occupational hazard among physicians. In Minnesota, drug addiction has been reported to be many times greater among physicians than in the general population. Figures from Europe show that 15% of known addicts are physicians; in Canada twice as many physicians become addicts as do members of the general public. Evidently, in regard to narcotics, education is not a safeguard. Rather, the problem is created and amplified by accessibility and availability.

Treatment projects, such as methadone, may help individual addicts. From a PUBLIC health standpoint, optimistic views regarding such treatments need qualification. Ostensibly such treatments remove users and pushers from the streets. Yet since the introduction of a large scale methadone program in New Haven, there has been a large increase of adolescent narcotics users. The question is whether heroin made available on the market looks

for new consumers, and whether, for every addict put on methadone—with the smaller doses needed in early stages—several new users may be inducted.

This is not to argue against the initiation of such treatment programs. Nevertheless, from a PUBLIC (not individual) health angle, little is achieved, if for every patient on methadone, several teenage novice addicts enter the drug scene.

As to residential treatments, both California and New York states have large scale programs for heroin addicts. In both, grave doubts have been expressed lately regarding their effectiveness. A recent report from California shows that despite commitments for a year, most addicts will relapse and return to the institutions repeatedly. After six years of experience with civil commitments in California, it appears that for most patients such programs do not achieve the expected success, and that new beds have to be made available at an increasing rate. In California, 300 beds have just been added and occupied, and another 450 beds are being made ready. In New York, recent reports indicate that the goals of civil institutional commitments remain unfulfilled, and that the original hopes attached to these programs have not been realized.

The impact produced by heroin dwarfs the other drug abuse problems, and since no immunization exists, the major efforts should be directed against this pathogen and its vector. Keeping such agents from susceptible individuals is one of the oldest and most reputable public health procedures known to medicine. It is the major preventive principle used in the control of such diverse diseases as malaria, lead poisoning or amebiasis.

A larger portion of the enormous sums spent for the treatment and residential care of heroin addicts should be directed to the organization of "search-and-destroy" actions against the pathogen, including isolation of its vector.

In syphilis or hepatitis one would not attempt to isolate some "original" source without going step by step backward through the chain of carriers. The same principle should apply to narcotics. It is commonly pointed out that the apprehension and incarceration of the little addict-pusher is of no value. However, it is he who infects the young novice, and it is he who, however uneducated, is

DR. HANS H. NEUMANN is Director of Preventive Medicine, Department of Health, City of New Haven, New Haven, Conn.

able to find without difficulty the intermediaries in the market. If these supplies come from other areas, then the job of epidemiology is not one for a local police, but for cooperative ventures of regional narcotics agencies. A city police, with its limited manpower, resources and liaison with state and federal agencies in this field, cannot possibly cope with the problem.

Recourse to policing and court action in the fight against disease is also an old public health prerogative. Quarantine and search powers vested by law in officers in this field are wide but might have to be broadened further. Police action may be unpopular at this time, but more training, more funds and more respect for it would be a prerequisite to justify other programs. This requires a cooperative venture of federal, state and city in task forces coordinated with a cadre of young detectives at the street level, who are well trained, with good monetary incentives. Ample rewards need be available for cooperation by the public.

There are cities in the U.S. comparable in size and population to New Haven, that have no heroin problem. The reason is not more education, immunity, or greater contentment, but the absence of accessible heroin. One may conclude that the prevalence of addiction in a community hardly depends on the receptiveness of its population.

When discussing drug addiction with teenagers in New Haven, they pose recurrent and disturbing questions: "Why do you allow narcotics to be sold on our street? Why is it so easy to get them?"

In combatting the narcotics problem, the first priority should be given to the search for the carrier. Along with this, more power is needed to follow the distribution chain to its source (epidemiology).

Otherwise, treatment programs hold a potential of tragedy for the community if for each addict entering treatment there is a chain of successors to addiction.

Reprinted from the Bulletin of The Connecticut Public Health Association, Hartford, Conn.

Portable Unit To Store Hearts For Transplant

(*Heart Research Newsletter*, 13: 1, 1969) Without a means of storage surgeons will use a heart taken from a donor no longer than an hour after death is declared. Dr. E. B. Diethrich working in DeBakey's laboratory now has a method for storing hearts. It is actually a heart-lung preparation much like the one used in physiology experiments. The preservation chamber is battery operated and completely self-contained with its own oxygen supply and respirator.

By this means human hearts have been stored for as long as nine hours and functioning well. Dog hearts have been preserved in such a chamber for longer than fourteen hours and have shown "excellent recuperability" when transplanted into another animal.—L.H.N.

"Yellow Light" For Steroids: Drugs May Be Overused

(*JAMA*, 209: 19, July 7, 1969) Arthritic deterioration continues painlessly under corticosteroid therapy, because persons who have jobs that are rough on their joints take steroids to get rid of their pain. Dr. Donald D. Weir's survey dealt with the order in which drugs are prescribed: salicylates, corticosteroids, indomethacin, phenylbutazone, gold and antimalarials.

The best treatment for most patients Dr. Weir believes is still a conservative regimen. This includes aspirin in sufficient amounts, rest, an exercise program and modification of the patients daily routine to relieve strain on the joints. In addition there should be "a philosophical acceptance that Rheumatoid disease lasts a long time."

Management of the chronic illness with a long range view of pharmacologic and physical therapeutic objectives and appropriate supporting therapy for attendant psychological problems was well done especially by certain internists and rheumatologists. It was the internist who generally spent more time with the patient, made more tests, kept better records and were more likely to refer patients for treatment at a medical center.

Patients were more likely to be advised about specific rest periods, than about limiting their physical activity or how to position their joints. "Apparently most physicians do not specify for the patients how much activities should be limited or how to recognize joint tolerance limits appropriately."—L.H.N.

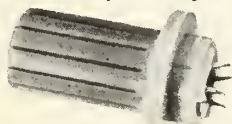
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The Talk Of The Convention

Quotes and notes made by Contributing Editors of MD'S WIFE who attended sessions of the AMA House of Delegates, interviewed picketing dissidents and participated in the work of the AMA Woman's Auxiliary's 1969 Annual Convention

At the AMA House of Delegates

Vice President Spiro Agnew: "I know that most doctors are interested only in practicing medicine, not playing politics. The nation is in sore need of perspective when opinion leaders nit-pick against a profession which in this century has added more than 20 years to life expectancy and has virtually eliminated so many crippling and debilitating diseases in this country and around the world. Our medical profession has achieved this, not our politicians and not our press."

Richard Kunnes, MD, third-year resident at Albert Einstein University, spokesman for demonstrators who invaded the opening session of the House of Delegates: "Let's get one thing straight. The American Medical Association is really the American Murder Association. You're the criminals who, rather than developing preventive health programs, have prevented health programs."

Roger O. Egeberg, MD, newly-appointed assistant secretary of the U.S. Department of Health, Education and Welfare: "The United States faces a crisis today in medical care due to the shortage in manpower, facilities and medical students. I understand that the average doctor works 65 hours a week and there are some who put in 84 hours a week. We have to think in terms of caring for the poor. We must find ways of distributing health care to them. Government must have the cooperation of the doctors to solve the problems."

Edward Martin, president of Student AMA: "Most MDs in practice are activists who wish to become involved in sane, carefully thoughtout change . . . All Americans, including the young, experience

strong feelings about certain problems which seem to arise with increasing frequency in these troubled times. Most of the students interested in them are leaders in their schools. The radicals are barely heard. Emotions among students and physicians are a good sign. Our profession is in peril when we are less worried, more complacent."

Along the Line of March of the Protesters

Medical students, young physicians, nurses and social workers, chanting and carrying signs, "AMA Go Away" . . . "Blue Cross-Double Cross" . . . "Hip Hip Hippocrates, Up with Service, Down with Fees"; "We are demonstrating to get health care for all . . . neighborhood centers should be in operation."

"AMA has not helped the medical students. Why don't they take some of the money they spend lobbying and help a fellow get an education? Student loan fund? I never heard of it. Why don't they tell us about such things?"

"I just finished medical school and have started my internship. I don't know anything the AMA is for. It's always anti . . . take Knowles for instance. Well no, I wasn't for him. It's just that the AMA shouldn't have been against him."

"All doctors' wives are interested in are mink coats and the country club."

"Well I guess the AMA has kept the standards of medicine high. I guess they've done some other things too, but I can't think what they are."

"Why doesn't the AMA use its effort and money to see that there is drug cost control . . . keeping the price of drugs down?"



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An MD's WIFE Reporter after talking to demonstrators: "How can youthful idealism be retained and channeled into the medical profession? Are they telling us something we should listen to? The heart and skill of our husbands go out in compassion to those who are ill and in the need of healing. Is there a breakdown in communications? Have they missed hearing about the many MDs who volunteer to go to foreign countries without pay? Or are they telling us to open our eyes to medical conditions at home?"

At the House of Delegates AMA Woman's Auxiliary

Mrs. John M. Chenault, president of the Woman's Auxiliary to the AMA: "Let us direct our energy toward achieving better health conditions and use our imagination in developing projects and programs which will meet the health needs of our communities . . . As we work with our medical societies, let us be ready to stand up and be counted as we speak with pride for those things which are right with American medical practice."

Ethel J. Alpenfels, PhD, professor of anthropology, New York University, keynote speaker: "If education has learned anything, it has learned that facts do not change attitudes. It is the principles, the concepts and the attitudes themselves that are the key. The medical profession today must begin to examine attitudes, its own as well as its patients."

Ann Landers, the world's most widely syndicated advice columnist and a member of the AMA's Advisory Committee on Health Care of the American People:

"Young people aren't worse than we were, only different. But that must be expected because the world has changed so much in the last 35 years. They have the disadvantage of too many advantages. Our culture has changed from the survival of the depression times to lack of motivation and new values . . .

"Being a wife of a doctor is a tough assignment, but wives of other professionals have the same complaint, the most universal being the lack of communication."

More than 500 delegates and auxiliary members: Repeating the Twenty-Third Psalm in emotion-choked voices at the memorial service where tribute was paid to Esther Long, the beloved, gallant leader who directed the activities of the auxiliary and had made all of the plans for the 1969 convention before her untimely death.

Reprinted from Md's Wife, July 1969

Woman's Auxiliary SEMI-ANNUAL LUNCHEON MEETING

Faculty-Alumni Center,
University of Connecticut
Storrs, Connecticut
MONDAY, NOVEMBER 3, 1969

10.00 A.M. Registration followed by semi-annual meeting and workshop meeting. There will be a social hour preceding the luncheon.

Reservation Chairman:

Mrs. Morton Arnold
Windham Center
Windham, Conn. 06280

Doctor's Office

Michael A. Dean, M.D., announces the association of Horace A. Laffaye, M.D. for the practice of surgery at 2660 Main Street, Bridgeport.

Donald A. Dworkin, M.D. and MacEllis K. Glass, M.D., announce the association of Jerold M. Perlman, M.D. for the practice of orthopaedics at 50 Ridgefield Avenue, Bridgeport.

Warren Heller, M.D., announces the opening of an office for the practice of medicine at 881 Lafayette Boulevard, Bridgeport.

Theodore Kramer, M.D., announces the opening of an office for the practice of ear, nose and throat and head and neck surgery at 10 Mott Avenue, Norwalk.

John J. McGarry, M.D. and James R. Dorr, M.D., announce the association of Edward Quinn, M.D. for the practice of internal medicine at 36 Old Kings Highway South, Darien.

Melvyn R. Ostrov, M.D., announces his association with William Cohen, M.D. for the practice of allergy at 83 Central Avenue, Waterbury.

David W. Parke, M.D. and William S. McClanahan, M.D., announce the association of Peter G. Burch, M.D. for the practice of ophthalmology at 477 South Board Street, Meriden.

OBITUARIES

Eric H. Blank, M.D. 1898-1969

Dr. Eric Henry Blank died on July 31st. He had been stricken ill while playing golf and was dead on arrival at Lawrence Memorial Hospital. The sudden death of Eric H. Blank came as a great shock not only to his family, but to his large circle of friends and the many patients for whom he had cared during his 35 years of practice in New London.



He was born in London, England, the son of Emil and Louise Blank. Dr. Blank was an Army veteran of World War I, serving in France.

A 1923 graduate of the University of Vermont, Dr. Blank was graduated from its medical school in 1925. He interned at Brockton Hospital in Massachusetts from 1925 to 1926, and in Danvers, Massachusetts.

Dr. Blank opened his practice in New London in 1926. He took a leave of absence to do post-graduate work in obstetrics and gynecology in Pennsylvania in 1937 to 1938 and served as a resident gynecologist at Graduate Hospital in Philadelphia in 1938 to 1939.

He had been affiliated with Lawrence Memorial Hospital since 1927. Dr. Blank advanced from associate, to senior, to chief obstetrician and gynecologist on the staff. He served on the medical advisory committee and education committee until August 1958, when he was named to the honorary staff. Dr. Blank became a member of the hospital consulting staff in January 1959.

In addition to being a Diplomate in obstetrics and gynecology, he was a Fellow of the American College of Surgeons, the American College of Obstetricians and Gynecologists; a member of the New England Obstetrical and Gynecological Society, the Knife and Stork Club, past president of the Connecticut Society of American Board Obstetricians and Gynecologists. Dr. Blank was a member of the Thames Club, the New London Rotary Club and the New London Country Club. The list tells only part of the story. To draw a complete portrait one should mention those rare qualities which made Eric so universally liked and admired. Quiet, unassuming, genuine, competent, loyal, generous, gentle, and devoted are some of the adjectives which come to mind. Yet these are inadequate words with which to describe a man whose passing leaves a gap which will be sorely felt by everyone who knew him.

Dr. Blank is survived by his widow, Nora Lasch Blank; a daughter, Mrs. Charles Farrell of Waterford; a sister, Mrs. William Eichhorn of Pike, New Hampshire, and three grandchildren.

F. W. Goodrich, M.D.

John J. Casagrande, M.D. 1906-1969

Dr. John J. Casagrande, of Pleasant Hill Road, Woodbridge, died suddenly on August 24, 1969. Dr. Casagrande was born in Genoa, Italy on June 17, 1906 and came to the United States as a very young child. He was educated in Seymour schools, graduating from Seymour High School in 1923. He re-



ceived his B.S. degree from Fordham University and his M.D. degree from St. Louis University. He interned and served surgical residencies at St. Louis County Hospital and The University Hospital of St. Louis.

Dr. Casagrande began general practice in Ansonia in April, 1937. He gave unstintingly of his time and talent and at all times his first thought was for the welfare of his patients and their families. In addition to general medicine and surgery, Dr. Casagrande had a large industrial practice.

He was on the surgical staff of The Griffin Hospital, Derby, and was at one time, president of the staff. Dr. Casagrande was a member of the Naugatuck Valley Medical Society, The American Academy of General Practice, the New Haven County Medical Society and the Connecticut State Medical Society. He belonged to the Elks and Knights of Columbus and was a member of Racebrook Country Club.

Dr. Casagrande is survived by his wife, Isabelle Silvey Casagrande, three sons, Thomas, John and James and a daughter, Carol Johnson. Also, four sisters, two brothers and thirteen grandchildren.

Wilbur H. Hansen, M.D.

In Memoriam

Backus, Harold S.—West Hartford, Long Island Medical College 1903. Dr. Backus was an urologist in the West Hartford area for many years. He was a member of the American Urology Society, the American Medical Association, Connecticut State Medical Society and the Hartford County Medical Association. Dr. Backus died July 17 at the age of 70.

Egan, John R.—Old Saybrook, Duke University 1942. Dr. Egan was a general practitioner in the Old Saybrook area since 1949. From 1944 to 1947 he served with the Army Medical Corps, and then became assistant chief medical officer at the national headquarters of the Selective Service System in Washington. He was an elected delegate of Middlesex County to the Connecticut State Medical Society House of Delegates from 1954-1960, and elected alternate councilor and then councilor from 1960-1968. Dr. Egan was a member of the American Medical Association, Connecticut State Medical Society, and the Middlesex County Medical Association. Dr. Egan died September 6 at the age of 53.

Garbelnick, David A.—Bridgeport, Boston University 1917. Dr. Garbelnick was a general practitioner in the Bridgeport area since 1928. Before his retirement he was on the staff of the Bridgeport Hospital and St. Vincent's Hospital. In 1967 he was honored by the Massachusetts Medical Society for 50 years of membership. Dr. Garbelnick was a member of the American Medical Association, Connecticut State Medical Society, Fairfield County Medical Association and the Massachusetts Medical Society. Dr. Garbelnick died August 28 at the age of 75.

Jones, Robert F.—New London, Columbia 1950. Dr. Jones was a psychiatrist in the New London area for the last four years. He was a retired Air Force lieutenant colonel. Dr. Jones was a member of the American Medical Association and the American Psychiatrists Association. Dr. Jones died August 29 at the age of 50.

Kirschbaum, Edward H.—Santa Barbara, California, Yale 1912. Dr. Kirschbaum was a surgeon in the Waterbury area for many years before retiring. He was very active in city holding public office on the Health Board and community organizations. Dr. Kirschbaum became commissioner of the Health and Medical Examiners for the city, he was the first chief of staff of Waterbury Hospital. Director of Surgery and Director of the Accredited Tumor Clinic at the hospital. He served in the U.S. Army Medical Corps as a captain in France and became surgeon director of the Army Hospital in France. Dr. Kirschbaum was a member of the American Medical Association, Connecticut State Medical Society, New Haven County Medical Association, New England Surgical Society, American College of Surgery and the American College of Gastroenterology. Dr. Kirschbaum died August 12 at the age of 80.

Middlebrook, Louis F.—Hartford, Johns Hopkins 1930. Dr. Middlebrook was a obstetrician and gynecologist in the Hartford area for many years. Director of the department of obstetrics and gynecology at the Hartford Hospital and consultant physician at New Britain Hospital, Windham Community Memorial Hospital, McCook Hospital and the Institute of Living. Dr. Middlebrook was a lieutenant commander in the U.S. Navy. Dr. Middlebrook was a member of the American Medical Association, Connecticut State Medical Society and the Hartford County Medical Association. Dr. Middlebrook died August 25 at the age of 65.

AROUND THE STATE

NEW HAVEN COUNTY

Board of Governors

New Haven County Medical Association

The Board of Governors of the New Haven County Medical Association met at the Colonial House in Hamden, on Thursday, August 28, 1969.

Fifteen new Provisional members attended the afternoon meeting to observe the workings of the Board. In the evening, after being indoctrinated as to the privileges and obligations of membership by a team led by Dr. John J. Mendillo, Chairman of the Committee on Credentials and Orientation, they were enrolled as Active members of the New Haven County Medical Association.

The new members are:

Jose Atocha, New Haven
Arthur S. Blank, Jr., New Haven
Malcolm B. Bowers, New Haven
Claudio Crupi, Waterbury
Terence C. Feir, Derby
John E. Fenn, New Haven
Amir H. Hemmat, Meriden
Etsuro K. Motoyama, New Haven
Franklin J. Nejame, Waterbury
Hans Neumann, New Haven
James M. Ozenberger, New Haven
William F. Quigley, Waterbury
Robert R. Rickert, New Haven

Dr. Henry Merriman of Waterbury was elected to replace Dr. Nicholas Preston of Waterbury on the Committee on Credentials and Orientation.

President Kurt Pelz and Dr. Hubert Bradburn were nominated as New Haven County members

of the Conn. State Medical Society Coordinating Committee on Charges.

Dr. Duane Anderson of Waterbury was elected as an Alternate Delegate.

The Board of Governors voted to become a supportive group for the "Citizens Against Lead" organization whose goals are the recognition and eradication of lead poisoning.

The Board of Governors declined to nominate a member to the Medical Advisory Board of CMS. Inasmuch as a recent communication from CMS alleged to be possibly misleading, President Pelz made it clear to the membership that the Clerk, Dr. West, was not now and had never been a member of CMS or any of its committees.

The Board of Governors voted to investigate the possibilities of county assistance to the Naugatuck Valley Medical Society in setting up a local public relations program.

A rather lengthy and somewhat heated discussion took place over the matter of achieving exact proportional representation on the Board of Governors according to the one man-one vote principle for each of the six geographical areas of the county. Some definition of the problem was accomplished, but a real solution was not reached at this meeting.

Our Councilor, Dr. Stewart J. Petrie, brought the members up to date on the recent proceedings of the Conn. State Medical Society Council meetings, and, along with Dr. Morris Granoff who is President-elect of the Conn. State Medical Society, and Associate Councilor Janes H. Root, Jr., answered numerous questions from the membership.

The Public Relations Committee is planning a poll of all New Haven County physicians regarding their attitudes about organized medicine, their willingness to participate, and their attitudes about public relations.

County office renovations at 362 Whitney Avenue have been approved by the Board, and along with previous measures already taken, should result in a more attractive as well as a more efficient enterprise.

Dr. Elliott S. Brand once again will direct the program for the semi-annual meeting of the Association to be held on Thursday, October 23, 1969 at the Waverly Inn.

Respectfully submitted,

William L. West, M.D., Clerk

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Ill Hearts Peril Drivers

(*JAMA*, 208: 2258, June 23, 1969.) Heart disease is the leading cause of death among motorists who die unexpectedly at the wheel and victims are often unaware of their condition so states Dr. Dominick J. DiMaio, a deputy chief medical examiner of New York City. He found coronary atherosclerosis in 41 of 47 such deaths. Four died of ruptured aortas and one suffered a thrombosis of the left internal carotid artery.

Few of the deaths resulted in serious accidents. The cars generally stopped after striking parked vehicles, trees or poles. Only 3 cars became involved in collisions. The majority of the drivers were between ages 50-69 who because of previous cardiac symptoms drive slowly, cautiously, pulling over to the curb as soon as cardiac symptoms are felt. This slow rate of speed brings the car to a stop with minor injuries to driver, passengers or pedestrians and also minor damage to car or object struck.—L.H.N.

Dreams May Increase Risk Of Angina In Heart Patients

(Heart Research Newsletter, 13: 3, 1969.) Dreams seem to increase risk of angina. Dr. J. Curtis Williams said his team noted changes in heart rate, the electrocardiogram, and blood pressure with an increased susceptibility to angina during dreaming.

There were 33 episodes of angina during dreaming and only 5 during non-dreaming sleep. Anginal events coincided with significant increases in pulse rate and blood pressure and changes in the electrocardiogram.—L.H.N.

Cholesterol-Reducing Drug Seems More Effective At Preventing Than In Reversing Heart Disease

(Heart Research Newsletter, 13: 3, 1969.) Dr. Abel J. Robertson, Jr. tried to determine whether clofibrate can bring about a reduction in mortality in men aged 30-64 who have had a coronary. In independent test-tube studies using single layers of human cells from the intima of arteries he found clofibrate on the surface of the cell preventing the cell from taking in fats. But it did not stimulate

release of fats including cholesterol already present in the cells.

He thinks it is a preventive agent in the treatment of atherosclerosis but that it must be begun at an early age since the drug does not reverse a lesion already formed.—L.H.N.

DDT: Criticism. Curbs Are On The Upswing

(*Science*, 164: 936, May 23, 1969.) Marti Mueller reviews what is happening to the DDT controversy since the seizure of 35,000 pounds of DDT contaminated Lake Michigan Coho salmon by F. D. A. There are of course pro and con forces to these actions, the latter from chemical manufacturers and farm groups. There is now an eleven member federal commission that Finch has named to begin study of the whole problem of water and soil pollution by DDT.

The recent government actions to limit or ban the use of DDT and to investigate the broad general effects of pesticide use in the environment could lead to whole new concepts about how pesticides should be used.—L.H.N.

About Heart Transplants: Survivorship Following Heart Transplantation In Canada

(Peter G. Gordon: *Canada Med. Assoc. Jr.*, 100: 1056, June 14, 1969.) What has been the cost in money and human suffering after heart transplantation? What has been the quality of life for those who survived the immediate post-operative period? What would survivorship be in a similar group of patients not receiving heart transplantation and what of its quality? Owing to heavy mortality following heart transplantation a temporary halt has been called to this procedure at the Montreal Heart Institute.—L.H.N.

Measles Eradication At Standstill. Cases Rising In Ghetto Areas

(*JAMA*, 209: 191, July 14, 1969.) Since the vaccine there has been a steady reduction in numbers of cases with the exception of 1964, the year of the Rubeola epidemic. In 1963, 450,000 cases were re-

ported; in 1964, 650,000; in 1965, 280,000; 1966, 226,000; 1967, 62,000; and 1968, 24,000 cases. This means we are running about 5 per cent of the pre-vaccination average.

Now Dr. J. Lyle Conrad expects a slight increase due largely to outbreaks in the "hard-core" ghetto areas of the east. However, these hard core areas have so many health problems that measles seems pretty small. Furthermore, they neither have the personnel nor the funds for efficient immunization campaigns. Dr. Conrad said who expects the struggle against measles to last at least 4-5 more years.—L.H.N.

Flu Pattern For 1970 Predicted: Type B To Upstage Hong Kong

(*JAMA*, 209: 195, July 14, 1969.) Only sporadic outbreaks of influenza caused by Hong Kong A2 virus strains are likely next winter, but Type B may occur in those parts of the country where the disease did not appear in 1968-1969.

Outbreaks of Type B influenza occurred last season throughout the central part of the country from Minnesota to Wisconsin to northern Texas. Few cases were reported from New York to New England.

The Public Health Service Advisory Committee on Immunization Practices recommended that only individuals in special danger groups should be vaccinated this year. Highly purified bivalent vaccines containing less non-viral protein, will be available. They recommend administration of vaccine subcutaneously in two doses, preferably six to eight weeks apart.—L.H.N.

Office Visit Leads Smokers To Quit

(*JAMA*, 209: 355, July 21, 1969.) Dr. Herbert Spiegel, a psychiatrist told the Section on Preventive Medicine that 20 per cent of 615 patients who sought his help have quit smoking for six months or more. The ingredients for success include; high patient motivation, one 45 minute session and a three point affirmative strategy in which the smoker reminds himself every one to two hours of what he is for, not what he is against.

Dr. Spiegel devised a session in which he helps the smoker set a positive goal. Essentially the patient is asked to relax and think about what Dr. Spiegel tells him. When the smoker is in a state of attentive concentration, he listens and repeats to himself the three-point goal: "For my body smoking

is a poison": "I need my body to live": "I owe my body this respect and protection."

When the smoker leaves the office he is asked to pause for twenty seconds every one to two hours and in a meditative shift of attention repeat these three ideas himself.

Dr. Spiegel believes that the conventional strategy of scaring is not very effective. Those who can respond to scare alone usually help themselves. Physicians are generally not convincing when they tell their patients they should cut down or quit. "We have not pushed ourselves to the limit to help people stop smoking and this direct impact method is a step toward the limit." The hard core turn out not so hard if we try at least once.—L.H.N.

Millions Of Children Need Psychiatric Aid

(*JAMA*, 209: 356, July 21, 1969.) Research discloses that 12-13 per cent of all American children have severe enough psychological problems from ages five through nineteen to require professional attention. During the 1970's at least 6-7 million children will require treatment.

If not detected early perhaps even by age three, these problems can result in permanent handicaps, Dr. Irving N. Berlin told the Session on Mental Health Dynamics in the Preschool Child. Physicians can and must play a vital role in heading off these handicaps. It is a mistake to believe children will outgrow their problems. We need 5 billion in funds to provide neighborhood centers, grants to train child psychiatrists and efforts of other agencies to cope with this sadly neglected field.

Poor nutrition can markedly affect the development of young children. Then there is the crippling effect of maternal deprivation which becomes irreversible by the age three. After this one can only try to repair some of the damage.

The main cause of the "failure to thrive syndrome" Dr. Berlin said was maternal ambivalence rather than total deprivation. Youngsters may feel unwanted, then fail to gain weight because they are likely to cry more and do not sleep properly.

When a child fails to reach clearly defined developmental landmarks the physician should look into the mother-child relationship to find ways of helping the mother, not only to relate to the child but help medically with some of the child's most distressing behavior.

Intervention that occurs early enough may permit reversal of the process.—L.H.N.

NEW BOOKS IN REVIEW

CURRENT THERAPY, 1969. Edited by Howard F. Conn, M.D. W. B. Saunders Company, Philadelphia and London. 945 pp. \$15.00.

Reviewed by: LOUIS H. NAHUM

The beginning and the end contain normal laboratory values of clinical importance. The author states that the book contains the latest approved methods of treatment for the practicing physician. This is undoubtedly true as one can see from the extraordinary efforts which the authors and editors have made to insure that dosage recommendations are precise and in agreement with standards officially accepted at the time of publication.

For the past twenty years this publication has brought to the practicing physician concise and specific discussions of current therapeutic procedures designed for ready application to the clinical problem at hand.

The articles have been written by physicians prominent in their respective fields and represent a careful distillation of the vast amount of information available for the therapist. The term "method of" merely reflects what the author would do if he had a particular disease to treat himself.

Each year *Current Therapy* is a new book. Of the 304 articles which comprise this one, 257 or 84.5 per cent are new and even those carried over from the previous year many have been carefully revised, so rapidly is biomedical science advancing.

The physician who uses this book is assumed to have an intimate knowledge of official announcements and official product circulars which should be followed. In some instances a larger dosage than that usually recommended is advised for patients under exceptional circumstances or in cases of serious or life threatening illnesses. In these instances the use of a dose or drug becomes obviously a matter of the physician's own clinical judgment.

To all who are engaged in practice this book is a must and could be referred to in almost every situation, simple or complex. Comparing this with previous editions it is not surprising how avidly the physician looks forward to each coming volume for he will find all the new ideas he needs every year.

MEDICAL SUPPLY IN WORLD WAR II. Edited by Colonel Robert S. Anderson, MC, USA and Charles M. Wiltse, Ph.D. Litt. D. and Contributors, Office of the Surgeon General, Department of The Army, Washington, D.C., 1968. 662 pp. with 149 illustrations, 54 maps and 8 tables. \$8.25.

Reviewed by: GERALD I. PITEGOFF

This thorough administrative history of the United States Army Medical Department covers medical supply in caring for 8 million people scattered all over the world during World War II. It encompasses every detail of this vast job which the Foreword to this book states included forecasting requirements for global war and planning procurement. It included the acquisition of raw materials, the construction of factories, and the creation of entire industries. It included

transportation from mines or farms or forests to processing plants; from plants to depots and from depots to the far corners of the earth, wherever American troops were stationed. It included the classification and selection of items and the packaging of these. More than 7,000 standard medical items and many more which were not standard, ranging from such diverse equipment as hospital beds to X-Ray machines and surgical needles had to flow in enormous quantities. This monumental task by many dedicated medical officers, who are named and given credit, is covered in this volume.

In the first chapter, which serves as a framework of reference for all succeeding chapters, the legislation for the procurement supply program which began in 1920 and was maintained until our entrance into World War II, is described. Because of the difficulties in medical supply during World War I The National Defense Act of 1910 charged the Assistant Secretary of War with the "supervision of the procurement of all military supplies and other business of the War Department pertaining there to the assurance of adequate provision for the mobilization of material and industrial organization essential to war time needs."

In addition to a clear discussion of the enabling legislation for the supply program, Chapter I covers the accomplishments in manufacturing facilities and training supply personnel along with the transition to war.

It was the contributors' and editors' opinion that the entire medical service for the United States Forces in the European theater of war being under one chief furthered the success of the program. This important fact is also included in the first chapter, as an overview of medical supply in the Pacific.

Chapters II-VI cover procurement and distribution of medical supplies in the Zone of the Interior; Chapters VII-XI are concerned with medical supply in the Zone of The Interior; Chapters XII-XVI with the war against Japan.

The appendices include medical depot information with a complete list of medical depots maintained by the United States Army, medical lend lease statistics, and a list of sample equipment.

There are illustrations showing equipment, bases and other items of medical supply interest. There are also photographs of the men who were responsible for the efficient medical supply service. There are many maps of medical supply depot systems. The careful work which the army did in the field of medical supply can well be illustrated by one small detail in demobilization planning. The adverse affect on small business by flooding the market with surplus Government stock at the conclusion of the emergency was taken into careful consideration and provision for releasing stock-piles was handled so as not to upset the economy. This and literally hundreds of other small but significant factors are covered and illustrate the depth of the work accomplished by the Medical Supply Department.

This book is an important addition to the Administrative Series published by the Historical Unit, United States Medical Service. May it never have to be used as a reference book.

MANUSCRIPTS

Manuscripts, including references or bibliography, must be typewritten, double-spaced on white paper 8½ x 11 inches with adequate margins on firm paper. The original copy, not the carbon copy should be submitted. Carbon copies or single spaced manuscripts will not be considered. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Receipt of manuscripts will be acknowledged and unused manuscripts returned. *Accepted* manuscripts become the permanent property of the JOURNAL and may not be reprinted elsewhere without permission from both the author and CONNECTICUT MEDICINE. The author is responsible for all statements made in his work, including changes made by the copy editor.

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The first page should list title, the author (or authors), degrees, hospital positions and any institutional or other credits. References should conform to the usual style of the JOURNAL (listing name and initials of author, title of article, journal, volume number, first and last pages and year), and should be cited numerically in the order in which they appear in the text; the number should be limited to the absolute minimum.

LENGTH OF ARTICLES

Ordinary articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of more than 4,000 words be published.

ILLUSTRATIONS

Illustrations should be numbered consecutively and indicated in the text. The number, indication of the top, and the author's name should be attached to the back of each illustration. Legend should be typed, numbered, and attached to each illustration as well as typed on a separate sheet. Photographs should be clear and distinct; drawings should be made in black ink (preferably India ink) on white paper. For half tones, glossy photographs should be submitted. CONNECTICUT MEDICINE will bear the cost of printing two cuts accompanying manuscripts submitted for publication. The cost of printing more than two cuts must be borne by the author.

NEWS

Our readers are requested to send in items of news, also *marked* copies of newspapers containing matter of interest to physicians. Letters intended for publication should be marked "For Publication." We shall be glad to know the name of the sender in every instance. All copy should be received one month prior to the expected date of publication.

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All advertising copy of products approved by the Advertising Committee of the State Medical Journal Advertising Bureau of Chicago shall be accepted for publication unless such copy is in conflict with official policies of the Connecticut State Medical Society. Non-Bureau advertisements in this issue have been reviewed and found to comply with the principles of advertising of the State Medical Journal Advertising Bureau, Inc. The acceptance of advertisements does not necessarily imply endorsement of any product or service by CONNECTICUT MEDICINE.

Material other than original articles should be received not later than the 10th of the month PRECEDING date of issue.

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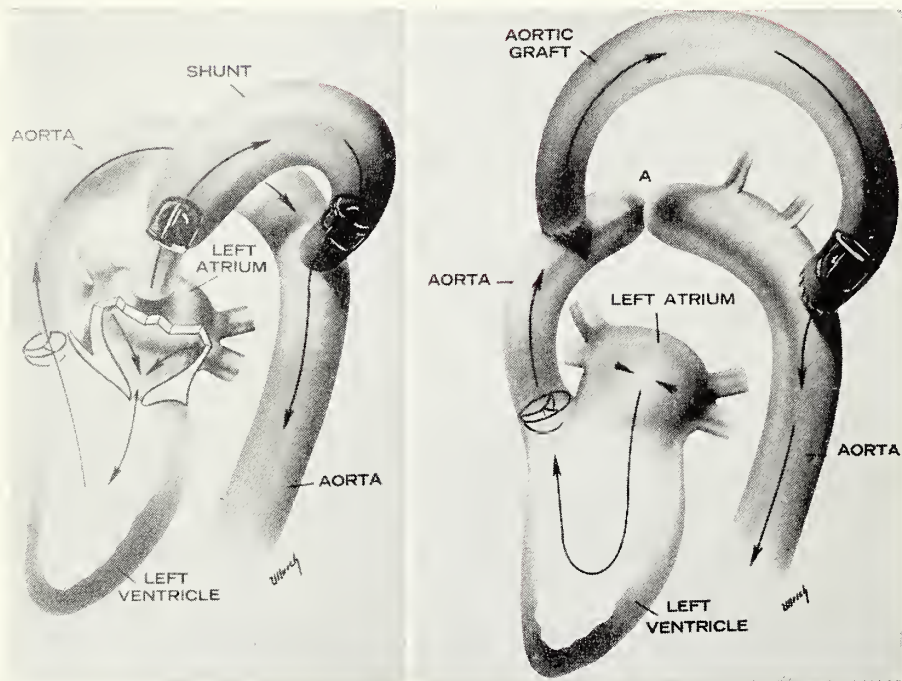
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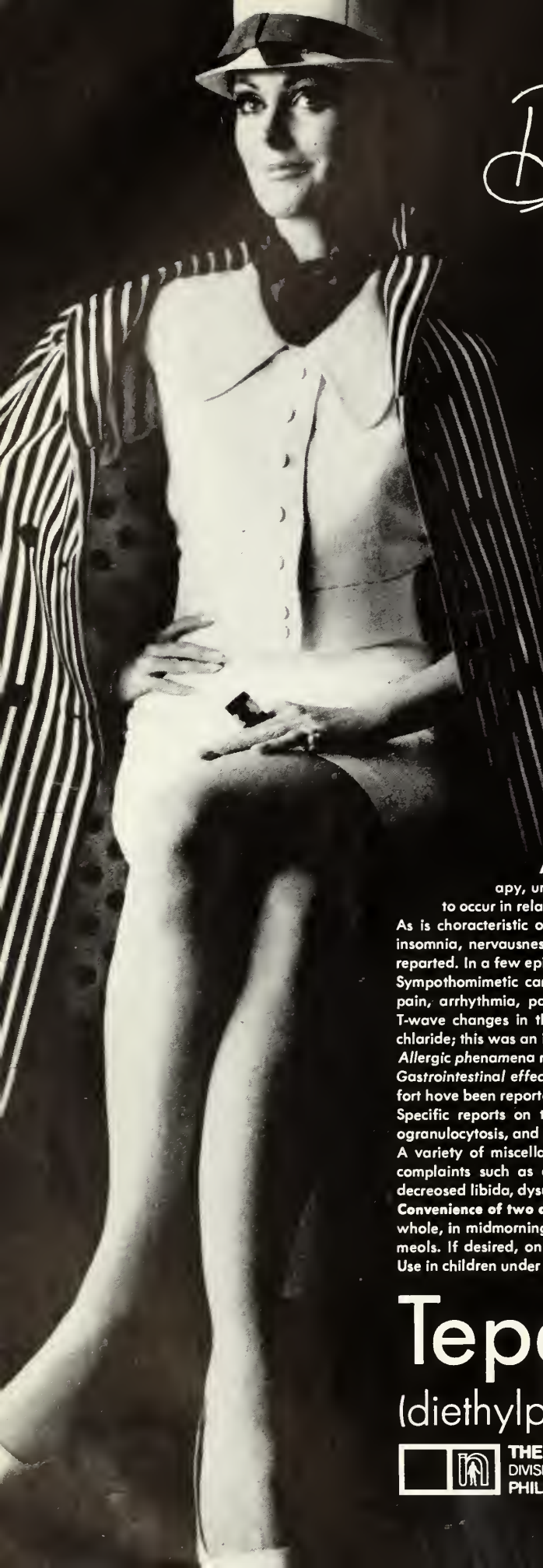
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Reflections About The Moon Landing

Six hundred million people viewed the landing on the moon and found there were no great surprises there. In fact, from orbiting spacecraft we already knew the moon's surface and from classical astronomy we were able to anticipate the departures from rotational symmetry of the gravitational field. By contrast Columbus did not know what he would find and Captain Cook was sailing to places unknown. Since Newton's time we know that seeing and touching are not essential parts of knowing. Confidence in the craft of model building is such that even distant parts of the universe or structures such as the helix of DNA have become a familiar part of understanding. Apollo 11 has done a great public service by providing a popular demonstration that there is no boundary to scientific understanding.

So what will happen next? There will, of course, be a program for the continued exploration of the moon. There will be several Saturn rockets and nuclear powered rockets will be pressed for. But the potential benefits of all this is far from clear. In spite of the excitement of the landing it is fair to say that in the space exploration of the past decade, the attainment of unmanned satellites have been greater, cheaper than anything which is promised by the programs which lie ahead. Earth satellites have discovered the magnetosphere, explored the solar winds, and prepared the way for a surge of interest in those phases of astronomy which are not possible on the earth's surface because of the obscuration of the atmosphere. It is probable that for several years to come instruments in earth satellites or planetary rockets would be a better buy than rockets for carrying people about.

It is also fair to say that there are many branches of science in which activities on the surface of the earth would yield scientific and social benefits more cheaply. Where strictly scientific considerations are concerned, the objective might well be to place more emphasis on old fashioned ways of investing money in research. NASA spent 30 billion on the moon adventure. It often seems a mockery that NASA should go on spending money while the mounting social problems remain unsolved. A part

of this mockery is the contrast between the 128 billion spent yearly on war and 2 billion spent on the poverty program and the serious cutbacks in support of medical education which has seriously unsettled the majority of medical schools in this country. Apparently relief of problems on this earth is less popular than exploration of space. This is why urban problems have lagged behind and not enough is known of the possible solutions to suggest that the money could be spent with confidence.

Having made space travel possible somebody must now show what it is for. Will it now be possible to change perspectives with which familiar terrestrial problems are regarded or will it obscure them further? Will it now be easier for rival nations to sink their differences? For example will disarmament be easier? Will poverty, national and international now be less respectable? History provides no solid ground for thinking that the pendulum will now swing right over and that this great accomplishment will indeed turn out to be a turning point in history, or a boon to mankind.

Dr. Thomas Paine believes that the arrival of space flight will work an intellectual transformation comparable with revolutions attributable to Columbus, Galileo, Newton and Darwin. That he should think in such hyperbolic terms is not surprising. After all he is the director of the space program. He has been talking about the ways his agency may be able to spread all kinds of benefits elsewhere in the world than just in this country. It is plainly the case that European Science has been helped along significantly by what has happened in the past few years. For many people, however, the acid test will be the extent to which it is now possible to work out some collaboration with the Soviet Union.

There is no denying that developments like these could profoundly alter the character of intellectual life. Certainly it would be dangerous at this stage to dismiss everything that has been happening as a futile prank, a way of spending large sums of public money. It is too soon to know. To say all this is not to crab spaceflight but merely to assert that it is one of those developments whose influence will depend on what use is made of it.

For those of us who are here it seems to have no purpose for the lives of the half-billion people who watched it. As physicians it seems less important than the cure of one case of cancer or the mysteries involved in the birth of a baby. If the monies spent on this adventure will deny universities their support and medical schools and hospitals their sustenance it could well lead to a decay of civilization rather than to its enrichment. We must not be blinded by glamour of which there was an excess supply on our TV sets. The priorities after all are our problems on earth.

L.H.N.

Effects Of Barbiturates On Dream Content

It is recognized that there are two kinds of sleep often called REM (rapid eye movement) and NREM (non-rapid eye movement sleep). These differ in their physiology and psychology. Awakenings from the REM sleep generally yields reports of dreaming during which there is vividness of the accompanying dream. Since barbiturates are a frequent sedative it is important to know what these drugs do to REM sleep. It has already been reported that barbiturates decrease the overall amount of REM sleep and reduce the progression of eye movements per minute. This has led to the prediction that administration of barbiturates would result in dream experiences of a more tranquil nature.

A corollary of this hypothesis would be that withdrawal of barbiturates should result in dream reports indicative of a richer and more vivid dream experience than in either barbiturate or prebarbiturate conditions. Oswald has shown that withdrawal of hypnotic drugs accentuates the progression of eye movements during REM sleep and leads to recall in the morning of vivid dreams during the night.

Carroll, Lewis and Oswald¹ have recently reported further on the effect of barbiturates on dream content. Three young men acted as subjects and each spent a total of 4 nights in the laboratory while the electrooculogram, electroencephalogram and electromyogram of each were recorded. They were given either 200 mg. phenobarbital or placebo. The dream reports were transcribed and given to two independent raters with instructions to rate dreams as "active" or "passive." The Foulkes scale which was used is an 8 point scale which attempts to indicate a progression from conceptual thinking

through perceptual thinking, to dream-like hallucination mental life.

Apart from scoring the reports as "active" or "passive" one of the raters also noted any dream containing marked sexual symbolism or content. The investigators found significant differences between the scores of the prebarbiturates and barbiturate condition as well as between barbiturate and withdrawal conditions. All three dreams considered sexual in theme occurred in the withdrawal condition. It was further found that the probability of obtaining an active report was different over all the conditions.

A probability test revealed that this difference lay wholly in the differential probability of a "passive" report between the placebo and the barbiturate condition. The withdrawal dream did not significantly surpass the prebarbiturate dream in vividness under the conditions of their experiment. One possibility is that barbiturates merely inhibit recall and that report of differences are due not to any difference in dream experience but to recall differences. This is unlikely in the light of Batten's findings that barbiturates actually facilitate recall.

Another possibility is that in the barbiturate condition it might take the subject "longer to come around." It has already been demonstrated by one of the authors that more gradual awakenings elicit reports of a more mundane and thought-like as opposed to dream-like nature. But in these experiments no difference in time lag between the first awakening stimulus and the first verbal response of the subject was discovered in any of the conditions. The conclusion from these experiments is warranted that barbiturates alter the dream experience making it more conceptual and less perceptual, more thought-like and less dream-like.

Carroll's results are relevant to many areas in medical practice in which barbiturates are used as hypnotics or sedatives. Since the dream-like state is essential to health and tampering with it by drugs or undue arousals can lead to disturbed mental function, hypnotics and sedatives that will not reduce REM sleep and its vividness should come to have an important place in therapy.

L.H.N.

Reference

1. Carroll, D., Lewis, S. A. and Oswald, I.: Effect of barbiturates on dream control. *Nature*, 223: 865, August 23, 1969.

The Problem Of Suicide

In this country suicide ranks as the tenth cause of death. One occurs every 24 minutes.¹ This figure

is likely low because the method of reporting and the existing medical and cultural taboos associated with suicide are not conducive to medical reporting. Suicide rates rise and fall depending in part upon socioeconomic factors. At the beginning of the century suicide rate was 11.3 per 100,000. In 1915 it was 17.9 but fell again to 11.5 in 1920. It rose again and reached a peak of 18.6 in the great depression of 1932. Slowly it dropped to a low point of 9.6 during World War II. Now it is back to where it was at the beginning of the century.

Suicide occurs in all classes of society although some differences in rates do occur among different religious groups. It does not necessarily occur in disturbed persons and there is no real evidence that suicidal behavior is inherited. A dangerous misbelief that is perhaps still held by a few is that people who talk about suicide are not likely to commit it. In fact studies have shown that probably over three-quarters of persons who attempt suicide have given previous warnings by talking about it or by talking about being helpless or dead, or simply "gone."

A recent technique has been developed in the study of suicide in very minute detail to determine what went into creating the suicide and what sort of signals the person gave that might have been picked up if someone had been listening and had become aware of them. Murphy and Robins in Resnik's book² have pointed out that physicians usually have opportunities to introduce the subject even though patients do not mention their suicidal preoccupations. One-half of the suicide in one series and three-quarters in another were known to have had medical and or psychiatric care within one year of their suicide and many of them within 3-4 months or less.

It is probable that many physicians do not question their patients about suicidal risk even though there is reason to believe that many patients would give this information if they were questioned directly about it. Since 70 per cent of suicides which Dorpat et al studied had active serious physical illness at the time of their death, it would appear that a large number of potential suicides do come into contact with a physician.

There are some criteria that are statistically valid in judging suicidal risk. Persons who have previously attempted suicide are obviously at greater risk. There is a compounding effect of age, sex and race. The incidence is lowest for non-white women under age 45 and increases progressively through white women under 45, non-white women

over 45, and non-white men under 45. Other factors correlating with high risk are separation, divorce or death of a spouse, being unemployed or retired, living alone, poor health, especially an acute or chronic illness in the six months preceding the attempt and a psychiatric disorder with mood or behavioral symptoms and especially alcoholism. The most lethal suicidal attempts are by hanging, use of firearms, jumping and drowning. A suicide note usually indicates that the attempt is more serious.

Karl Menninger³ mentions three motives for suicidal acts; the urge to die; to kill others or to be dead. To these one might add are the urge to gamble with life, to appeal to others, to be alive after death, to see how sorry others are, or to join a loved one in the hereafter. Newer ideas about depression expand upon the early Freudian concept that depression is due to introjected rage, directed at a lost (real or symbolical) love object which is still part of the mourning person. These concepts are of value in understanding and management of depressed and potentially suicidal patterns.

Suicidal prevention centers are becoming very common. The best known is the Los Angeles Suicide Prevention Center which was created in 1958 and which has contributed much original observations and research on this subject. In other plans there are community efforts which involve the medical profession usually psychiatrists as well as several other community resources and persons including volunteers. However, non-medical agencies have taken an active part in the field. This has resulted in some unfortunate competition for control or domination of the organizational structure of these centers. In two Canadian cities¹ debates have occurred between medical and social organizations as to whether the center should be administered as a social or even pastoral agency or as a medical and hospital-based service.

There exists much evidence that patients who are suicidal risks can be cared for in the wards of a general hospital provided there is careful management by a properly trained medical team. Regardless of when a patient is treated and how his psychiatric state is managed medically, a genuine and close relationship between him and his helper is very important. When his helper is a physician as is usually the case he must be emotionally mature and have adequate knowledge of the patient as well as of all aspects of suicide. Psychotherapy of some kind should always be part of the treatment. The

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relationship with a physician beginning early and maintained during a suicidal crises is of definite help.

Initial psychotherapy need not be complicated. The physician simply has to be uncritical, accepting and concerned. He must also be resourceful enough to ensure that there is proper help given by family and others and that all potential methods of suicide are removed. He will be assisted greatly in his handling of the suicide patient if he is aware and convinced that there is much about suicide that is predictable and preventable.

Current information about the prediction of suicide and the management of potentially suicidal patients is presented in a recent book entitled "Suicidal Behavior."² The volume to which 48 authors have contributed is probably the most extensive and adequate collection of papers thus far offered on the subject. One cannot read this book without realizing that there is much available information on the subject of great benefit to all physicians who are concerned with the problem of suicide.

L.H.N.

References

1. Prediction and Prevention of Suicide. *Can. Med. Assoc. J.*, 100: 867, May 10, 1969.
2. Resnik, H. L. P., Editor. *Suicidal Behavior: Diagnosis and Management*. Little, Brown and Co., Inc., Boston, 1968. p. 49, 57, 163, 209, 190.
3. Menninger, K. A.: *Man Against Himself*. Harcourt Brace and Company, Inc., New York, 1938.

The Health Center Movement: II.

New health centers are now being sponsored by hospitals, medical schools, citizen's group, medical societies and less often by health departments. Under new sponsorship these centers are developing at the same time as group practice which is a kind of private health center and receives a stamp of professional and public approval. Another health center movement in mental health quite separated from medical practice has also developed. The district is now viewed not just as a community but a laboratory where the effect of "health" care can be measured as an independent variable. Here they think of studying the social basis of health and sickness and how much it will cost.

This seems promising but has definite limitations. It may arouse community fears of manipulation similar to only recently discarded ones of "being a guinea pig" in public hospitals and resentment at being "over-researched" whereas in suburbia the personal physician devotes his life in

the best interest of the patient. There are justifiable fears that the monies for such centers may fall into the hands of extremist leaders who will not use them in the best interest of the patient. Then there is the fear that programs of health centers once established may not be resistant enough to change as public needs change, and the physician patient-relationship becomes essential.

In still another modern view the district is losing its geographical boundaries because the clientele of a health center or group practice may become larger and centers with it because of more efficient transportation. If boundaries disappear and the centers grow in size and complexity, then community participation, traditionally based on small groups will be more difficult and certainly some will be left out. If they are sponsored more by hospitals they may become as out-patient divisions often have "colonial" outposts and the major resources again held by hospitals.

The idea of participation is back again. The center's governance and control is democratic by having local residents and consumers represented as advisors sometimes being the majority of the centers board of directors. Participation by residents now also has assumed a new meaning. In the old health centers, services were brought to the poor so that they could become healthy. However, they remained poor just the same. The new center idea offers the poor jobs and training as a part of a comprehensive program for their social, economic, educational, as well as medical rehabilitation.⁷ The philosophy behind this is that medical rehabilitation by itself is unfeasible.

The jobs are in and outside the center. Residents may work outside in the neighborhood as aides, helping increase the centers use or in community "store fronts" as "patient advocates" resolving conflicted encounters with the center. Residents may have a real professional job or human relations work introducing the personal touch by guiding patients through the center's services and so removing impediments inherent in depersonalized bureaucratic treatment. Besides paid jobs and training and having a say in the agency's goals, is the idea of participation in everyday management. Today the center's staff may also take part in the new industrial democracy in management decisions,⁸ a practice now considered no longer based on political theory. There is great psychological advantage of this, for the staff to have a voice in the goals of the organization as well.

THE BREAKUP of a business partnership, the crack-up of a marriage, the shake-up of being fired or reduced to bankruptcy... after any significant loss or severe blow to self-esteem, *both* anxiety and depression almost always follow.



What must not be forgotten is the danger of bureaucratic organization which develops a life of its own and in search of efficiency can easily lose sight of the social needs for which it was created. Encounters with patients suggest that neither efficiency nor bureaucracy alone is the answer to full medical care. Patients may be indecisive about even seeking help. They may be awkward in coping with illness. The course of their illness may be uncertain and its management and treatment equally so. They need a personal physician to guide them and in this set up he may not be available. The bureaucracy of a health center may not make best use of the psychosocial treatment of the patient's illness and rehabilitation. Its efforts may be less efficient than its expansive nature.⁹

The new community health problems are not as so commonly perceived simple, but quite complex whether they are those of the very young-infant mortality, or those of the old chronic psychosocial medical disease and disability. The new programs seek prevention of illness, rehabilitation of residents, the search for optimal functioning and achievement. But in both objective and costs the programs of centers is uncertain and the programs are quite unlike private-office medical practice, to which they are often compared. Uncertain also is the primacy of the center's community programs over the demands of hospitals.

Speaking about the Columbia Point Neighborhood Health Center, Gibson¹⁰ expresses the repeated hope that the health center not the hospital would be the focus for the reorganization of medical care and that its program and social orientation would be that of medicine and of medical education. At present they are certainly not so. The technological therapies and orientation of the modern hospital are much more impressive and command more resources. It is possible to foresee a change in the hospital's priorities for care. Then the health center, public or private may begin to develop resources to deal with complex problems of health in the communities.

Private or public, the health center can become the long idealized center for medical care. Not so easily will it become a place for the renewal of the community and for the rehabilitation of the poor. These last two aims are concerned with disorders of society and will have to be solved by society itself.

With the virtual conquest of infectious diseases through antibiotics and immunizations, medicine and medical science have changed and is entering

an era in which understanding and studying of personality problems has become essential to scientific advance. For a goodly number of the errors committed by physicians involve failure to recognize the emotional origin of symptoms. The resolution of such errors requires an ability to work with emotionally disturbed patients and to become able to understand what can cause such disturbances and how they can be ameliorated. The health center's interest is in environment and elimination of disease, the physicians interest is in people, a desire to help them, a wish "to stand with the patient against his fate," and help him to avert tragedy and when one cannot, to help provide the strength to bear it.

The eradication of so many diseases during the recent past has not diminished the importance of the physician as a person and he is turning more time and attention to problems of living rather than preservation of life. The patient expects when he places himself in a doctor's hands, his health and welfare will be of primary importance to the physician whose prestigious place in society is exactly because he places the patient's welfare on a par with his own. He continues to do whatever lies within his ability, simply because the patient came to him in his role as a physician.

This personal relationship between patient and physician will become ever more important and the health center movement will fail as it has in the past unless provision is made somehow for the preservation of this priceless medical heritage.

L.H.N.

References

7. Geiger, H. J.: Tufts Comprehensive Community Health Action Report. Boston, June 23, 1966. (Mimeographed)
8. Bennis, W. G.: Changing organizations: Essays on the development and evolution of human organization. New York, McGraw-Hill, 1966.
9. Anderson, O. W.: Health services in land of plenty: In environment for man: The next fifty years. Edited by W. R. Ewald, Jr. Bloomington, Indiana, Univ. Press, 1968, pp. 59-94.
10. Gibson, C.: Beyond group practice. Presented at 10th annual family health lecture, Children's Hospital Medical Center, Boston, March 13, 1968.
11. The Person. Theodore Lidz. Basic Books, 1968.

How To Fight Destruction Of Our Environment: The E.D.F.

The question is whether we Americans have a constitutional right to a clean and healthy environment—to freedom from pollution. Everyone knows who is doing the polluting, vested interests, local governments who are unwilling to enforce ordi-

nances and uninterested in the public good, administrative agencies whose inspectors represent the industries they are supposed to regulate, people in general who will drive badly adjusted motors and pollute our air and many others. How can this grave ecological problem be tackled? One way is through legal action.

An organization that is doing something about environmental pollution is Environmental Defense Fund (E.D.F.) in Long Island, New York, consisting of a small group of lawyers and scientists who joined forces two years ago to bring about effective pollution control through legal action. Court hearings make excellent platforms for airing scientific data and scientists can make excellent witnesses to confront the polluters. It is an article of faith with E.D.F. that professional scientific societies although well meaning are essentially ineffective in fighting pollution. They have no way of confronting their opponents with tested data. However, individual members have been approached and asked to testify in areas of their expertise. The response of the scientific community has been "overwhelming," said Professor Charles Wuster of the State University of New York, Stony Brook who is a trustee of E.D.F.¹

The idea for E.D.F. grew from a suit Mr. Yannacone filed in 1966 in behalf of his wife and "everyone else" entitled to the natural resources in Suffolk County. The action was brought against Suffolk County New York Mosquito Control Commission to enjoin it from spraying the area with DDT. Mr. Yannacone a frustrated research neurophysiologist, now a lawyer, brought several life scientists in to testify on the harmful effects of DDT. Technically Yannacone lost the case since the Judge ruled that although he had proved that spraying with DDT had actually contaminated the environment, an action to bar the insecticide would have to come from the state legislature. In effect, however, Yannacone did win his point. The publicity attracted by vigorous condemnation of DDT led eventually to the suspension of DDT spraying by the Mosquito Control Commission.

The process of accumulating tested scientific data on the harmful effects of DDT has led E.D.F. to what could be its most important suit to date, actions it is planning against the U.S. Department of Agriculture; first to force it to open for public scrutiny its now closed pesticide registration file, and then to compel cancellation of the registration of DDT as a commercial pesticide.

Under the Department's existing rules manufacturers of commercial pesticides must file a registration statement which consists of data concerning the ingredients, safety and effectiveness of the chemicals in question before the pesticide can be licensed for sale in the United States. However, the Department unlike the F.D.A. does not challenge or check the data in the statement. Licenses are granted on the evidence furnished by the manufacturers and the registration statement is not open to public scrutiny. The registration statement for DDT was filed in the early 1940's long before there was any knowledge about its serious harmful effects by Geiger Chemical Corporation which held the patent. The registration has never been reviewed or opened to the public. E.D.F. hopes not merely to force a revocation of the registration of DDT but also to force a change in the registration procedures of the Department so that the evidence about chemical agents submitted for future licensing will be examined and questioned as carefully as drugs are now by F.D.A.

E.D.F.'s biggest battle so far is to force Wisconsin to declare DDT a state-wide pollutant. The organization was brought into Wisconsin by three conservation groups of which one, the Michigan Audubon Society is helping to defray the costs. The test case which is not brought for money damages but to improve the environment was opposed as might be expected by the manufacturers of DDT. Nevertheless E.D.F. proved without any doubt that DDT is a pollutant and is causing severe damage to the environment. More than a dozen young scientists gave impressive evidence for E.D.F. that DDT has caused population collapse among carnivores, birds, is causing problems of reproduction in fish, of enzyme induction in rats and is interfering with neural signal transmission in crabs. Even more scientists than took the stand were waiting to be called, a total of over 250 had offered to testify against DDT. The same effects that occur in crustaceans might be produced in humans and unlike other toxic agents and anesthetics, the effects of DDT are irreversible according to Professor Alan Steinback, a young neurophysiologist.

In Michigan, E.D.F. forced 55 cities to stop spraying with DDT and instead substitute less harmful pesticides. The State Agriculture Department stopped recommending DDT and outright ban on its manufacture is to take effect this year. In 1968, E.D.F. initiated a suit against a large pulp mill which it charged with pollution in the area. An-

other of the Group's big actions concerns the ecological disruption being caused by the Trans-Florida Canal currently under construction by the U.S. Army Corps of Engineers. The suit will be against the engineers on behalf of the ecosystem of the State. Another of their plans is to help a Colorado Conservation group prevent the take-over of fossil beds by land developers.

E.D.F. policy is formulated by a board of trustees which is made up in part of biologists, life scientists and the National Audubon Society. It will not limit itself to a single chemical agent or any one kind of pollution. It will move wherever the environment is being degraded. It will need local organizations to pay the cost and scientific support. As would be expected with such a public spirited organization, its financial condition is always shaky. Thus far The Rachel Carson Fund has supported it. Hopefully major foundations will change their neutral attitude and support it. It deserves mass support from everyone.

L.H.N.

Reference

1. Sheldrick, M. G.: E.D.F. vs DDT: Scientists fight pollution. *Scientific Research*, August 4, 1969.

Vitamin D And Calcium Serum Levels

As a result of two major advances, the metabolic fate and mechanism of action of vitamin D has now been clarified. One method was the synthesis of ³H-labeled vitamin D of high specific activity and the other was new methods of extraction and chromatography which permitted separation of vitamin D and the products of its metabolism.

Orally administered vitamin D is primarily absorbed in the jejunum¹ in a process requiring bile. After absorption the vitamin enters the lymphatic system and most of it is carried in the chylomicron fraction of the blood stream. It then enters the liver where its metabolites become tightly bound to albumin, alpha-globulins and lipoproteins in stable and non-ultrafiltrate form.

The major part of an orally or parenterally administered dose appears very early in the liver. Much also appears in the skeleton, muscle, blood, liver and kidney. Its highest concentration, however, is in the skeleton and intestinal mucosa, the major target organs for the effects of vitamin D. The gastrointestinal tract appears to be the major route for excretion of the vitamin and its metabolites. They pass through the bile into the gut, thereby providing an enterohepatic circulation and

fecal excretion. Few of the metabolites and no unaltered vitamin D per se normally appears in the urine.

One of the metabolites is capable of curing rickets and also increasing serum calcium concentration by stimulating active transport of calcium in the intestine. This has been demonstrated in animals deficient in vitamin D. It acts on bone, mobilizing calcium. It is much more effective than vitamin D itself. This can be inferred from the fact that there is a time lag between the administration of vitamin D and the appearance of the physiological effect presumably because it takes time for the formation of the biologically active metabolite (25 hydroxycholecalciferol). The conversion of the vitamin to its biologically active form may occur to some extent in the small intestine. However, the major site of activation of vitamin D is probably the liver.

After the appearance of large amounts of the active vitamin in the intestinal mucosa it then requires another interval for the D metabolite to participate in an induction process. This probably consists of the synthesis of a calcium binding protein in the intestinal mucosa which is required for the calcium transport system in the intestine.

The serum calcium level we now see is not only a function of the parathyroid hormone, but can also be lowered by any mechanism that results in reducing calcium absorption from the gut. It is generally recognized that glucocorticoid administration may diminish calcium absorption in-vivo and there is a well known clinical antagonism between the effects of steroid hormones and vitamin D. Hypercalcemia and hypercalcinuria have been reported in a fair proportion of patients with sarcoidosis, nephrolithiasis, nephrocalcinosis. Even renal failure can occur. This defect in calcium metabolism is due to excessive intestinal absorption of calcium. Corticosteroids may dramatically lower serum calcium levels in such cases and also in vitamin D intoxication probably by reducing calcium absorption. Corticosteroids also reduce the serum calcium in patients with idiopathic hypercalcemia of infancy, a condition believed to result from excessive intake of vitamin D. Finally corticosteroids effectively prevent replacement therapy with vitamin D in hypoparathyroid patients.

It is probable that vitamin D may be necessary for the action of parathyroid hormone on the intestine and bone. The known antagonism between the adrenal and parathyroid gland can be attributed to the antivitamin D effect of cortisone.



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By the two new methods mentioned above we have learned in what way the active transport mechanism of calcium in the intestine is dependent upon vitamin D and how glucocorticoid administration appears to be "antagonistic" to those of vitamin D. Furthermore, in cases of calcium deprivation, there develops a compensatory mechanism whereby there is an increase in the level of the vitamin responsive calcium binding protein which enhances active transport. This is probably why patients on very low calcium intake are nevertheless able to maintain normal serum calcium levels.

L.H.N.

Reference

1. Kimberg, D. V.: Effects of vitamin D and steroid hormones on intestinal calcium transport. *New Eng. J. Med.*, 280: 1396, June 19, 1969.

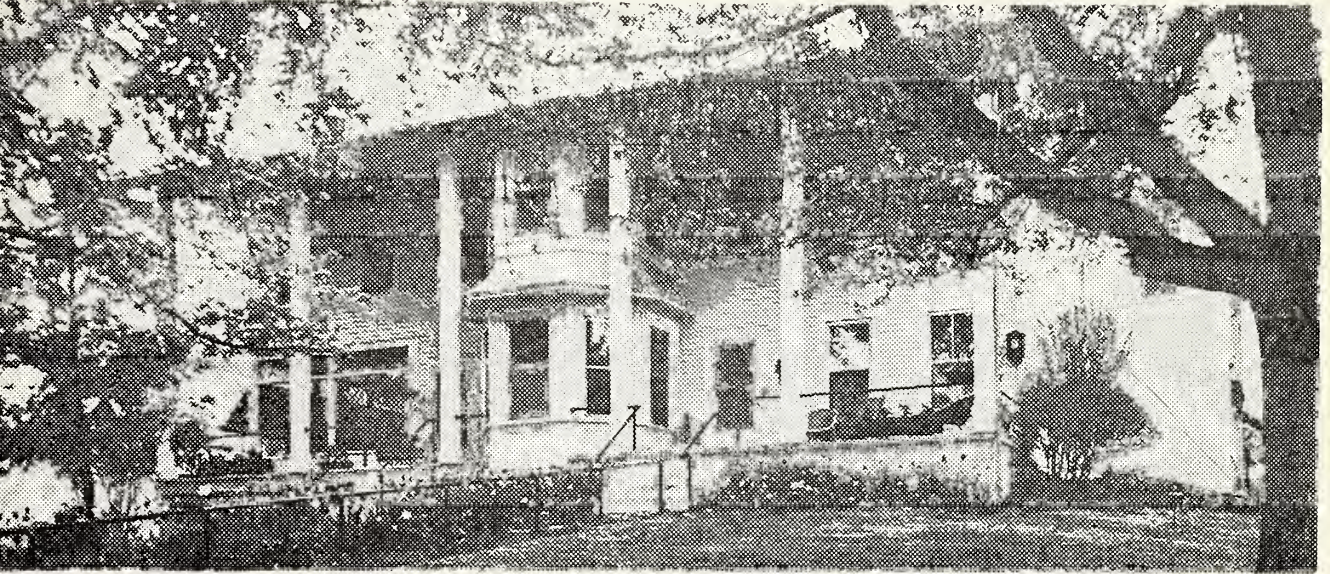
**The Role Of The Uterine Cervix
In The Reproductive Process**

It appears that the role of the uterine cervix in the reproductive process is more subtle and complex than suggested by earlier investigators. This came out at a Conference on Fertility and Sterility held in Jamaica, January 3-12, 1969. The quantity and the biophysical and biochemical characteristics of cervical mucus are under endocrine control. The amount of mucus increases progressively during the follicular phase of the sexual cycle and at ovulation it is profuse and watery. During the latent phase, cervical mucus is scant, viscous or gelatinous and opaque. Such mucus is much less favorable for sperm survival than during the follicular phase.

Massive numbers of sperm adhere to cervical mucus. The successful completion of fertilization and frequency is related to the biophysical and biochemical characteristics of the mucus and the pattern of its accumulation around the internal and external os at the time of insemination. The site of the sperm reservoir within the female reproductive tract depends on the site of ejaculation of the species. In some species the semen is deposited in the vagina or cervix (for example primates, ruminants and rabbits) the uterine cervix acts as the sperm reservoir and regulates the release of sperm from the mucus in the uterine lamina.

In some where semen is deposited within the uterus, the uterotubal junction rather than the cervix acts as the sperm reservoir. Bovine sperm penetrates the cervical mucus within 1-4 minutes and is then transported from the cervix to the site

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of fertilization within a few minutes. Mechanical stimulation of the cervix and the external genitalia causes rapid transport of the sperm. Little is known, however, about the effect of cervical stimulation on the release of oxytocin and subsequent uterine contraction and sperm transport. Further research is needed to understand the role of the cervix in reproductive failure.

Cervical mucus of humans and bovines contains two mucoids with different molecular size and electrophoretic mobility. Hydrolysis reduces their viscosity which in turn results in an acceleration of germ migration. The variability of the conductivity of the cervical mucus is related with the time of cycle and therefore hormonal status. Patients taking oral contraceptives show different peaks than the normals whose peaks or conductivity maxima coincide with the mid proliferative and early secretory phase.

It appears that the viscosity and surface tension of cervical mucus are of considerable value in studying ovarian function and ovarian disorders. The proteinogram of mucus for example is of great diagnostic value in cases of cervical pathology. If there is no infection, there are tests that reveal the physiological status of the endocrine glands and therewith the adequacy of the cervical mucus and its secretions for sperm migration. Where cervical hostility exists, there may be no abnormality of hormone production, but sperm transport through the canal may be prevented by antigen-antibody reactions reflecting immunologic incompatibility between the sperm and female tissues.

We know that some of the external secretory glands (salivary, nasal, lacrimal) secrete antibody locally in the form of gamma A globulin. The uterine cervix is similar physiologically to these glands in that it serves as a barrier preventing the bacteria of the vagina from entering the uterine cavity. The vagina also has been suggested as being capable of local antibody production against sperm possibly affecting subsequent fertility. The ingredients necessary for the local production of antibody are present in the cervix. Further studies are needed to document the possibility of stimulating the cervix to produce antibodies locally.

If the cervical secretions involve local antibody production in a manner similar to the lacrimal or nasal glands, there may be significant clinical implications regarding involuntary infertility among married couples as well as the possibility of utilization of this mechanism for inducing voluntary infertility as a method of conception control.

M. Roland reported that micro-dose administration of norgestel a synthetic progestogen without estrogen effectively prevents conception in women. These contraceptive effects may be due to pharmacological interference at the cervical level with possibly sperm capacitation. Capacitation involves morphological, biophysical and biochemical maturational changes in the ejaculated sperm in the female reproductive tract. This phenomenon is well documented in the rabbit although not demonstrated in other species including primates. The possible role of the cervical mucus in sperm capacitation in man is of particular interest in view of the following phenomena: There is a fair amount of mixing between the seminal plasma and the cervical mucus during coitus. Pockets of sperm penetrate the mucus due to differences in surface tension. A large volume of semen escapes from the vagina after withdrawal. Further studies are needed to evaluate the role of cervical mucus in sperm capacitation.

Oral administration of 17 aceto-progesterone compounds causes 2 antifertility effects in the rabbit. At one dose spermatozoal transport is inhibited at the cervical and uterotubal junction and fertilization is prevented. At a lower dose the eggs are fertilized but implantation is inhibited. The 19 norprogesterones at comparatively high doses inhibit ovulation by direct effects on the ovary. However, at lower dose fertilization is unaffected but implantation is prevented (J. B. Bennet, B. H. Vickery, R. I. Dorfman).

The hope of course is that contraceptive methods may be developed which are based on shortening the survival time of sperm in the cervical canal, or altering the processes of sperm maturation or capacitation. New modern methods of fertility control through blocking sperm migration and fertilization will markedly improve the effectiveness of family planning programs.

The next World Congress on Fertility and Sterility organized by the International Fertility Association will be held in Tokyo, October 17-25, 1971.

L.H.N.

Reference

1. Hafetz, E. S. E.: Uterine Cervix. *Science*, 164: 334, April 18, 1969.

The Bethesda Conference On Early Care For The Acute Coronary Care Suspect

The acute coronary patient if he has an arrhythmia and reaches the hospital has a better prognosis today than did his counterpart a decade ago. At the same time Kuller et al¹ have pointed out 60



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Zinc (from Zinc Oxide)	0.25 mg.
Iodine (from Potassium Iodide)	0.25 mg.
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Manganese (from Manganese Sulfate) ..	0.5 mg.
Magnesium (from Magnesium Sulfate) ..	0.5 mg.

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per cent of all arteriosclerotic heart disease deaths occur outside of hospitals. Similar figures apply to those who died of coronary artery disease.² The major task then is to do everything we can to prevent coronary atherosclerosis in the general population by well recognized methods of eliminating the risk factors: obesity, hypertension, diabetes, gout, hyperlipemias including triglycerides and hypercholesterolemia and especially smoking. These are all removable and once achieved would go a long way to reduce the acute attacks that bring patients to the hospital and the sudden deaths that occur outside the hospital.

This preventive approach is a long term one and in the meanwhile what do we do with those patients well advanced in their disease and approaching sudden death, since approximately 60 per cent of all deaths from coronary heart disease occur within one hour of the onset of symptoms? It would seem that this loss of life might be reduced if heart attack suspects were to request and receive the benefit of modern care more promptly than they do. This entire problem and its solution if one exists does not rest with the patient alone, since many sudden death victims apparently had tried to obtain assistance. Kuller estimated that as many as one-quarter had visited a physician sometime during the seven days preceding death. A part of the difficulty may lie in the ability of medical personnel to separate serious from less serious complaints. For example those with arrhythmias are much more prone to die suddenly even in the absence of a new coronary closure. Of course, in the presence of an arrhythmia quick aid might well save such a person if it were available. It would have to be quick, however, for as we have seen above most die within one hour of the attack.

At a recent Bethesda Conference on "Early care for the acute coronary suspect" it was generally agreed that more must be known about the events which precede sudden death before large scale programs can be designed to prevent it.³ Some investigators thought that more needs to be known about the effect that social and economic factors have on the coronary suspect that leads him to either seek or not to seek medical aid. The assumption here is that if we could induce people to go to their doctor, that somehow he could anticipate which person will drop dead from an arrhythmia and take steps that might be successful. Some participants wondered about the importance of the patient's beliefs and knowledge of the symptoms, treatment, and prognosis of acute heart attacks. It

was believed that frequently the denial of serious symptoms blocks the patient's ability to summon help.⁴ Factors influencing the patient's behavior cannot be the sole determinants of early care. Emergency care, personnel facilities and coordination also must be carefully examined to determine how they can be improved.

The conference produced several recommendations, some of which can be widely carried out immediately at relatively low cost. These include improved emergency room procedures for handling heart attack suspects, more widespread deployment of defibrillators and education of the subjects regarding symptoms, treatment and prognosis of acute heart attacks. Ideally the disease should be perceived by the patient as a threat serious enough to initiate action but not serious enough to cause denial of the possibility of a heart attack.

Certain other avenues were considered that may be promising but require careful evaluation before general use can be recommended. These include use of mobile CCU,⁵ electrocardiographic telemetry and defibrillation by specially trained paramedical personnel. Some general recommendations of the conference called for further investigation including an examination of factors which influence the patient to seek medical care, safer prophylactic antiarrhythmic agents for ambulatory patients with coronary artery disease and better diagnostic techniques to discover the patient with an impending coronary.

It is, however, doubtful that these measures by themselves will make a serious dent in overall mortality from coronary atherosclerosis although it surely should save some individual lives. Even such a notable innovation as the CCU itself has not significantly reduced the overall mortality from coronary disease. Clearly our greatest task is to search for the risk factors in our patients and take urgent steps to eliminate them.

L.H.N.

References

1. Kuller, L., Lilienfeld, A. and Fisher R.: An epidemiological study of sudden and unexpected deaths in adults. *Medicine*, 46: 341, 1967.
2. Vital Statistics of the United States. Vol. 2, page 278, 1958.
3. Bethesda Conference Report: Early care for the acute coronary care suspect. *Amer. J. Cardiol.*, 23: 603, 1969.
4. Olin, H. S. and Hackett, F. P.: The denial of chest pain in 32 patients with acute myocardial infarction. *JAMA*, 190: 977, 1964.
5. Pantridge, J. F. and Geddes, J. S.: A mobile intensive care unit in the management of myocardial infarction. *Lancet*, 2: 271, 1967.

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Improving Life Expectancy In Patients Who Have Recovered From Myocardial Infarction

The notion that survivors of an infarct most often died of another one led to long term anticoagulation as a possible way of improving long term survival. In addition to the assumption that deaths resulted from new closures in a coronary artery were other assumptions also. One was that new attacks were thrombotic in origin and therefore anticoagulants should be able to prevent them. There are two fallacies in this simplistic view that deaths in coronary heart patients occur from a new thrombus in a coronary artery. One is that almost half of all coronary closures are not due to a thrombus at all but rather to a subintimal hemorrhage. The second fallacy is the belief that the dynamics in the formation of an arterial thrombus are identical with that in a venous thrombus and that the same prophylaxis will prevent either. We now know that an arterial thrombus is made of a platelet mass which is not prevented by anticoagulation treatment.¹

What then are the causes of death among survivors of myocardial infarction. There have been difficulties in answering this question because of the absence of comprehensive or fully representative post-mortem examinations. To try to overcome this difficulty a group from Melbourne Australia² has approached the matter by stating criteria by which the modes of death of all their patients could be classified. The 86 deaths occurring in this trial were distinguished as occurring suddenly, after chest pain or in other ways. The findings were that most deaths were either sudden or after chest pain, that deaths after chest pain were fewer than expected and that the proportions of sudden deaths was the same whether or not the patient was on anticoagulation.

Few of the reports of other trials provide full information on modes of death. However, of six authors analyzed by Lovell, the results reveal a pattern similar to that described in the Melbourne study. The same was observed by Leren³ on 206 survivors from myocardial infarction (MI) treated with cholesterol lowering diets. They seemed to suffer fewer MI than the control subjects but their risk of sudden deaths remained the same.

These observations provoke a number of thoughts. First the idea that the commonest cause of death after recovery from MI is questionable because many, perhaps half, of these patients die suddenly.

Unlike patients dying soon after developing symptoms of MI, in those dying suddenly there are frequently no signs of recent thrombosis or infarction even with the most thorough postmortem examination. We must not confuse sudden death with MI. The second point is that the mode of action of anticoagulants is irrelevant to the mechanism precipitating the sudden deaths.²

We are led to two considerations in approaching the problem of preventing deaths in the patient who has recovered from MI. One is properly controlled trials of diets such as Leren used, and drugs such as those affecting platelet adhesiveness that might diminish the tendency to recurrent thrombosis in arteries. The other approach is an evaluation of measures which might diminish the tendency for sudden death to occur. The mechanism of sudden death, other than when it is precipitated by coronary occlusion, recurrent infarction or rupture of the ventricle, is thought to reflect sudden disturbances in contraction of the heart resulting in ventricular fibrillation or standstill. The Melbourne study suggests that patients at particularly high risk of sudden death may be detectable in advance.

Twenty per cent of patients with major arrhythmias noted in the hospital died suddenly during a follow-up of three years as compared with only 7 per cent of those who had not had an arrhythmia noted. Whether the risk is related to some arrhythmias and not others requires detailed follow-up of many more patients. At the same time the stage is set for controlled trials of long term prophylactic administration of such antiarrhythmic drugs as seem safe to test in a post-infarct group. What is apparent is that coronary artery disease patients who exhibit rhythm disturbances are in need of close supervision.

Since the increased risk of death in patients who have had an arrhythmia with their acute episode is chiefly in the first 12 months after discharge from the hospital and since their mortality in this period is about 30 per cent² the duration of such trials and the number of patients needing to be studied to evaluate therapy is not forbidding.

It would be idle to suppose that the life expectancy statistic for patients who have recovered from acute MI will be the same as for the general population. Many of the patients at risk have recovered well from their acute illness and have hearts such as have been described as "too good to die."⁴ A

decrease in the number of sudden deaths after leaving the hospital will, therefore, further increase the life expectancy statistic for such patients.⁵

L.H.N.

References

1. Nahum, L. H.: Factors in the formation of the white thrombus. *Conn. Med.*, 31: 599, September 1967.
2. Lovell, R. R. H.: The prevention of late deaths after myocardial infarction. *Am. Ht. J.*, 78: 1, July 1969.
3. Leren, P.: The effect of plasma cholesterol lowering diet in male survivors of myocardial infarction. *Acta Med. Scandinav. (Suppl)*, 446, 1966.
4. Beck, C. S. and Leighninger, D. S.: Hearts too good to die. *Ohio M. J.*, 56: 1221, 1960.
5. Adelsen, L. and Hoffman, W.: Sudden death from coronary disease. *JAMA*, 176: 129, 1961.

Support Of Heart Action

Three methods have been devised thus far to assist the circulation. In the first, the work of the heart is lessened by reducing the amount of blood that the ventricle must eject. A second device alters the pattern of aortic pressure so as to reduce the afterload of the left ventricle and increase the

diastolic pressure. This is termed pressure-assist or counterpulsation. The third approach also uses the principle of counterpulsation but augments the stroke volume of the pump with blood drawn from the venous side. It is this hybrid procedure which it is hoped will offer a solution to one of the major difficulties in applying counterpulsation to patients in cardiogenic shock.

In counterpulsation a major artery is cannulated and the cannula is attached to an actuator. Blood is alternately drawn from and returned to the arterial tree in synchrony with systole and diastole. The pumping is so phased that the pressure at the root of the aorta is reduced during systole and elevated during diastole. The triggering of this maneuver can be the R wave of the electrocardiogram or ascending limb of the aortic pressure curve. This method reduces left ventricular work and therefore oxygen need from coronary flow. It also may stimulate development of collateral circulation. Even though this process is slow, nevertheless studies on coronary shock preparations have revealed in fact that counterpulsation is a potent stimulus to the development of coronary collaterals.

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Ordinarily less than 30 per cent of coronary flow occurs during systole and over 70 per cent during diastole. When diastolic pressure is elevated by counterpulsation coronary flow will increase. Similarly reduction in systolic pressure produced by counterpulsation permits greater coronary flow also during systole because of decreased extra mural pressure upon the coronary vessels. This is why this method has been recommended as a treatment of cardiogenic shock induced by myocardial infarction. The effect of synchronous assist on heart failure is still uncertain largely because the type of heart failure and the associated atherosclerotic lesion found in man are not readily reproducible in laboratory animals.

One evolution of this method is to increase blood volume by taking various blood from the vena cava via femoral vein, oxygenate it extracorporeally and then returning it during diastole into the arterial system by counterpulsation. The method increases stroke volume, produces greater elevation of diastolic pressure and minimizes the amount of hemolysis resulting from fluttering of the vessels.

Another modification is introduction of a non-occlusive balloon via the femoral artery into the aorta. The advantage is said to be that no blood is handled outside of the body and only the aorta is cannulated. It does, however, require heparin to prevent clotting around the balloon, trauma to the aortic intima and interference of flow to branches of the aorta are problems not yet solved.

Counterpulsation involves invasion of the vascular system, use of an extra corporeal blood handling device, sterile precautions, administration of anticoagulants and use of anesthetics. For these reasons synchronous external assist was advanced as a procedure that would be free of trauma and could be applied for long periods. It involves external pressure applied to the lower body or legs varied in such a way as to provide assistance to the left ventricle. Distribution of blood is controlled and the venous return and cardiac output augmented.

Soroff et al¹ with a rigid three section chamber provided rapid control of external pressure and allowed the ambient pressure to be increased or decreased. Synchronization again was controlled electronically with the R wave. A similar device by varying pressure applied to the external chest wall by a curas can reduce work of the right ventricle by 30 per cent.

Heart disease not correctable by medical or sur-

gical means should ultimately require an artificial pump. Presently implantable devices capable of assisting the left ventricle for long periods are being developed for clinical use. With one type of device blood is collected from the left atrium and pumped into the aorta by passing the left ventricle. A second device is based on the concept of counterpulsation. Blood is pumped from the ascending aorta to the descending aorta during diastole in synchrony with cardiac action (see front cover). Soroff's group is also experimenting with a subcutaneous prosthesis capable of assuming the pumping action of the left ventricle. This requires a long graft anastomosed to the side of the ascending and descending portion exteriorized in the subcutaneous tissue.

The method of counterpulsation was used in seven patients with cardiogenic shock for periods from six to forty-eight hours but only one of the seven survived. Kantrowitz² had a better survival rate of 40 per cent in fifteen patients with cardiogenic shock, an improvement over the previous experience in which only 10-20 per cent of patients with cardiogenic shock survived. The external synchronous pressure assist was used in two patients both of whom succumbed. The same result was found in two patients with implantable chronic assist devices.

Experimentation is continuing. Veno arterial pulsatile by-pass is being tried as is synchronous left atrial to femoral by-pass. Finally is the paracorporeal prosthesis for chronic assist devised by Dr. Liotta.³ This is the type used by Dr. Denton Cooley on his famous patient Haskell Karp who lived sixty-five hours with it. Clot formation in the prosthesis remains as one of the major problems associated with chronic implantation of assist devices and needs much experimentation to overcome.

Despite the imaginative and prodigious efforts of many investigators as well as the commitment of many granting agencies to develop mechanical systems and techniques for treatment of heart failure it is apparent that the indications for assisted circulation are still uncertain and clinical methods for applying these experimental procedures are far from perfected. It appears that the clinical use of certain forms of assisted circulation should at present be limited to these patients who are clearly beyond any other means of therapy and are at a terminal stage of illness.

Further advances in this field will require intensive basic research of the physiologic problems as

well as the more obvious technical refinements of the equipment.

L.H.N.

References

1. Soroff, H. S. et al: Physiologic support of heart action. *New Eng. J. Med.*, 280: 693, March 27, 1969.
2. Kantrowitz, et al: Clinical experience with cardiac assistance by means of intra aortic phase-shift balloon pumping. *Tr. Am. Soc. Artif. Int. Organs*, 14: 344, 1968.
3. Liotta, D. et al: Prolonged partial left ventricular by-pass by means of intrathoracic pump implanted in left chest. *Tr. Am. Soc. Artif. Int. Organs*, 8: 90, 1962.

Early Detection of Bone-Marrow Injury Due To Drugs

One of the most serious adverse effects of drugs is depression of the bone marrow. With some drugs, timely studies of the formed elements of the blood permit early recognition of bone-marrow injury and help forestall irreversible damage. Frequently, however, the sudden onset of chills or fever, acute inflammation or ulceration of the mouth or throat, bleeding, anemia, profound weakness, or collapse is the first indication of drug-induced hematologic injury.

Toxic Bone-Marrow Depression—Commonly-used drugs having a direct toxic effect on the bone marrow include most of the anticancer drugs and the phenothiazines. Anticancer drugs usually inhibit the proliferation of all bone-marrow elements—granulocytes, lymphoid cells, platelets, and erythroid cells. The adverse bone-marrow effects of anticancer agents are usually predictable, and when the drugs are withdrawn, are usually reversed. Cessation of therapy is obviously not necessary, however, when the therapeutic aim is depression of activity of blood-forming organs, as in leukemia and polycythemia. The frequency of blood tests during therapy should depend on the relative toxicity of the agent and the intensity of therapy.

Agranulocytosis occasionally complicating the use of the phenothiazines, especially chlorpromazine (Thorazine), mepazine (Pacatal), promazine (Sparine), and thioridazine (Mellaril), usually becomes apparent between the tenth and the sixtieth day of treatment; agranulocytosis rarely occurs with short-term or intermittent use. In its early stages, phenothiazine-induced agranulocytosis is frequently asymptomatic and may be discovered only if a blood count happens to be made. A. V. Pisciotta (*JAMA*, 208: 1862, June 9, 1969) performed weekly leukocyte counts for the first two months of therapy on

6,200 patients taking phenothiazines. Only five cases of agranulocytosis were identified before symptoms developed. Phenothiazine-induced agranulocytosis is reversible when the drug is discontinued and rarely progresses to aplastic anemia.

Chloramphenicol-Induced Aplastic Anemia—The mechanism of hematologic injury induced by chloramphenicol (Chloromycetin) is uncertain; both toxic and hypersensitivity factors may be involved. The manufacturer recommends that a complete blood count be done every other day for the duration of therapy. Frequently, however, aplastic anemia will not be discovered early enough to prevent irreversible damage. Furthermore, the disorder may appear weeks after chloramphenicol therapy has been stopped. The Committee on Adverse Drug Reactions of the California Medical Association and the California State Department of Public Health state that because of the risk of aplastic anemia the use of chloramphenicol “. . . appears totally unwarranted for treating minor conditions, for prophylactic therapy, or for treating infections if a safer alternate drug is available” (R. O. Wallerstein et al., *JAMA*, 208: 2045, June 16, 1969). When chloramphenicol is used, the patient should be under careful clinical surveillance for symptoms of blood dyscrasias both during and for many weeks after administration of the drug.

Hypersensitivity Bone-Marrow Injury—Drugs occasionally causing hypersensitivity disorders of the bone marrow or peripheral blood elements include aminopyrine and dipyrone, quinacrine (Atabrine), phenylbutazone (Butazolidin) and oxyphenbutazone (Tandearil), quinine, quinidine, sulfonamides, the thiouracils, gold salts, trimethadione (Tridione), and, rarely, the tricyclic antidepressants (imipramine [Tofranil], amitriptyline [Elavil], and others).

In some hypersensitivity drug reactions, a single dose of a drug can produce a precipitous drop in the leukocyte count a few minutes after administration. With other drugs, reactions may occur only after days or weeks of continued or intermittent therapy. With many of the drugs that can cause blood dyscrasias, careful clinical observation is probably more important than periodic blood counts. Equally important, the patient should be alerted to report any symptom of a blood dyscrasia (see first paragraph).

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Cardiovascular Effects of Psychotropic Drugs

Michael H. Ebert, M.D., and Richard I. Shader, M.D.

Abstract

The cardiovascular actions of the major classes of psychotropic drugs are discussed. The phenothiazines, tricyclic antidepressants, and monoamine oxidase inhibitors can all produce hypotension. When substances with amine radicals are administered along with monoamine oxidase inhibitors, hypertensive crises can occur. The phenothiazines, particularly thioridazine, produce definite and predictable changes in the electrocardiogram. Arrhythmias have been reported in patients receiving phenothiazines and in cases of imipramine overdosage. Various precautions and considerations of drug interaction should be observed in administering psychotropic drugs to patients with cardiovascular disease.

Introduction

In recent years important cardiovascular actions of the major psychotropic drugs have been recognized. Some were unknown when the drugs first entered clinical use. The mechanisms of these effects are complex and often not fully understood. In this, the eleventh article in our series, we review the cardiovascular side effects of the major psychotropic drugs in use today. Also considered is the use of psychotropic drugs in individuals with cardiovascular disease. To an increasing extent psychotropic drugs are being used in the management of patients with cardiac disease. In such patients major and minor tranquilizers must be chosen carefully with regard to their specific cardiac actions and to other actions that might effect cardiac function. The discussion will focus on the phenothiazines and the anti-depressants since these agents have significant and common cardiovascular actions.

Effects On Blood Pressure And Pulse

The most common cardiovascular effects of phenothiazines and antidepressants involve blood pressure and its regulation. The minor tranquilizers, in therapeutic doses, rarely effect blood pressure or pulse. Although the effects of psychotropic drugs on blood pressure are general clinical knowledge, studies in man that document them are few and in general inadequately controlled. Such studies are usually done on chronic, patient populations, and not on normal subjects. An example of the difficulties that this population selection raises is illustrated in the recent study by Bishop and Gallant.¹ They demonstrated greater lability in blood pressures of schizophrenic patients on no medication or on an inactive placebo drug as compared with normal subjects. The validity of this finding is somewhat in question. The patients studied had been off phenothiazines for only six weeks, and it is possible that the lability of blood pressure could be accounted for by the continued mobilization of phenothiazines from fixed tissue stores. At any rate, the study suggests a source of error in reporting the incidence of hypotension in a group of treated patients, without including the blood pressure measurements of a control population.

It is generally accepted that phenothiazines cause hypotension, particularly postural or orthostatic hypotension. Hypotension is more frequent and severe with the aliphatic and piperidine groups of phenothiazines (e.g., chlorpromazine and thioridazine) than with the piperazine group (e.g., trifluoperazine).² The clinical studies of hypotension have generally been done with the aliphatic group of compounds, usually chlorpromazine. The findings differ with respect to acute, subacute, and chronic administration.

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Several anesthesiologists have studied the acute administration of phenothiazines to surgical patients in a supine position on an operating table. In one study³ doses of 25 to 50 mg of chlorpromazine were administered IM or IV to 185 patients. There were no fluctuations in pulse, but in 13% of the patients systolic blood pressure dropped 40 mm

or more. In another study⁴ IM administration of 25 to 50 mg of chlorpromazine caused an average fall in systolic blood pressure of 14.5% in 10 conscious subjects and 12.7% in 16 anesthetized subjects. A transient rise in pulse rate was noted in some subjects. Many animal studies demonstrate a moderate fall in systolic blood pressure after the parenteral administration of chlorpromazine. The constancy of the effect varies among species.⁵

Most clinical studies of the effects of phenothiazines in man are subacute, with the drug administered over a period of weeks. Generally, in these studies, hypotension is not noted as a side effect. However, in many of them the technique of measuring blood pressure is not standardized from subject to subject. The orthostatic component of hypotension, (i.e., the change in blood pressure from lying to sitting or lying to standing position), is rarely measured. A large study on the side effects of phenothiazines by Hollister, *et al.*,⁶ found that significant changes in blood pressure were rare. Whether blood pressures were standing or supine, however, is not mentioned; and no standard technique of measurement was described. Blumberg,⁷ studying 114 patients of mixed diagnoses, found that chlorpromazine did not effect supine blood pressure after six weeks of treatment. By contrast, Sommerness, *et al.*,⁸ found that chlorpromazine administered over 12 weeks to 33 highly disturbed psychotic patients caused an average fall in blood pressure of 20 mm systolic and 10 mm diastolic. Unlike the previous two studies, a placebo group was included. The systolic and diastolic blood pressure fell in this group also, but the change in chlorpromazine treated patients was significantly greater (.01). Some of the differences in these studies can be explained by the fact that the hypotensive effect of phenothiazines, when administered subacutely or chronically, is largely orthostatic. Korol, *et al.*,⁹ in a carefully controlled study, administered chlorpromazine for 30 days to schizophrenic patients. He found that sitting and standing mean arterial pressures were significantly depressed when compared to placebo, but that no significant change occurred between the groups when the blood pressure was taken in the supine position.

In spite of the fact that phenothiazines are often administered to a patient for months or years, there are practically no studies of the chronic effects of phenothiazines on blood pressure or pulse. One study was performed by Sletten, *et al.*,¹⁰ on 14 schizophrenic patients who took oral chlorpromazine (10 mg/kg) for 90 days. Chlorpromazine tended

to decrease supine systolic blood pressure. The decrement reached statistical significance on the 10th, but not on the 30th or 90th day.

The mechanism by which phenothiazines cause hypotension is not clearly understood. It has been demonstrated in animals, and questionably in man, that phenothiazines cause vasodilatation. This appears to be mediated by a direct effect on the arterial wall and also by central mechanisms. In man two plethysmograph studies have shown increased blood flow in the hand following brachial artery injection of small amounts of chlorpromazine.^{4,11} In one study,⁴ after placement of an arterial needle in the brachial artery and a control infusion of saline, 1/80-1/6 mg of chlorpromazine was injected per minute for 5 minutes. Blood flow in the test hand was compared with the flow of the opposite hand, to control for spontaneous fluctuations. The arterial infusion of chlorpromazine in four subjects caused an average increase in flow of 50% in the infused hand, suggesting a local vasodilatory action. An intravenous infusion of 25 mg of chlorpromazine in eight subjects caused an increase (of nearly 300%) in blood flow in the hand, which was interpreted as suggesting a central inhibitory action on vasomotor tone. There is considerable evidence in animal studies that chlorpromazine has a central depressant effect on vasomotor and respiratory centers when injected intracisternally, intraventricularly, or into the vertebral artery.⁵ Intracisternal injection of chlorpromazine also depresses cardiovascular reflexes, such as the pressor response to carotid occlusion or afferent vagal stimulation.^{12,13} Finally chlorpromazine has a sympatholytic or alpha adrenergic blocking effect. It reverses the pressor effect of epinephrine and decreases its positive inotropic effect.

Patients who develop hypotension from phenothiazines generally do not develop a shock-like syndrome. The hypotension can usually be treated by placing the patient in a reverse Trendelenburg position. *Epinephrine should not be administered* since it may further lower blood pressure. The phenomenon of epinephrine reversal has been described many times in man and animals since it was first noted by Courvosier in 1953.¹⁴ It consists of a paradoxical hypotensive reaction to epinephrine after the administration of chlorpromazine. The frequency of occurrence of epinephrine reversal is related to the dose of chlorpromazine and is more frequent when the drug is administered parenterally.¹⁰ This effect has been explained by the hypothesis that chlorpromazine has alpha adrenergic

blocking properties which permit the full and unopposed expression of the beta adrenergic (vasodilating) properties of epinephrine.⁵ The patient who is hypotensive because of phenothiazines is more subject to cardiac arrhythmias, probably because of the unopposed stimulation of beta receptors. Because of this it has recently been recommended that such patients be treated with propranolol, a beta blocker, as prophylaxis against dangerous arrhythmias.¹⁵ This use of propranolol, however, is still investigational. Severe hypotension and the development of clinical shock can be treated with norepinephrine using doses sufficient to overcome the alpha blockade. The patient's fluid and electrolyte balance must be kept in mind when administering phenothiazines, especially to elderly patients. A patient who has a decreased vascular volume from acute hemorrhage, dehydration or treatment with diuretic agents is more prone to the hypotensive side effects of phenothiazines.

The antidepressants also have hypotensive side effects. Klerman and Cole,¹⁶ in a review of the pharmacology of imipramine, state that postural hypotension and tachycardia are noted in about 5% of all cases. Lunn and Kristiansen¹⁷ report a higher incidence of hypotension with therapeutic doses of imipramine. Of 85 patients with endogenous depression, 45 had an average fall of systolic blood pressure of 20-30 mm. Muller, *et al.*,¹⁸ reported a similar incidence of postural hypotension in a study of 82 patients on imipramine, 41 of whom had evidence of coronary artery or hypertensive cardiovascular disease. Forty-seven patients developed postural hypotension. The hypotension was mild in 27 patients, moderate in 10 patients (complaints of dizziness and drop in diastolic pressure of 10-20 mm), and severe in 10 patients (evidence of moderate shock or syncope and drop in diastolic pressure of greater than 20 mm). The patients with severe hypotension all had concomitant cardiovascular disease, whereas mild hypotension was equally distributed between patients with cardiac disease and the group without cardiovascular problems. The propensity of imipramine and other tricyclic antidepressants to produce serious cardiac effects in patients with pre-existing cardiac disease will be further discussed below.

Animal experiments with imipramine^{19,20} show that small doses of imipramine in cats and dogs (less than 2 mg/kg IV) increase blood pressure and rate and contractility of the heart.¹⁹ This effect is interpreted as a sensitization of adrenergic receptors to norepinephrine, perhaps mediated by blocking

reuptake of norepinephrine into the presynaptic neuron. Large doses of imipramine in animals (2-5 mg/kg) cause hypotension and decrease myocardial contractility, heart rate, and coronary flow. Sigg¹⁹ interprets these phenomena as a negative inotropic effect of imipramine on the myocardium, while Cairncross, *et al.*²⁰ feel that imipramine in larger doses shortens diastole and impairs cardiac filling—thereby decreasing cardiac output.

The second large class of antidepressant agents, the monoamine oxidase inhibitors (MAOI), has a complex interaction with blood pressure mechanisms. The MAOI can all produce hypotension, particularly postural hypotension. The hypotensive effect resembles that produced by sympathetic blockade.²¹ Some MAOI have been used as anti-hypertensive agents.²²⁻²⁴ A study by Oates, *et al.*,²⁵ found pargyline to be equal in clinical efficacy as an antihypertensive agent to guanethidine and alpha methyl dopa. *Hypotensive crises can occur when MAOI are combined with diuretic agents.*

The mechanism of the hypotensive effect with MAOI is not certain. A current theory implicates the storage of false neurochemical transmitters in the sympathetic nerve ending during monoamine oxidase inhibition.²⁶ These endogenous amines, such as octopamine, have a less active effect than norepinephrine on the receptor site when released by sympathetic nerve impulses.

The most serious cardiovascular complications of MAOI are hypertensive crises. When the MAOI were first introduced, these attacks occurred with a frequency of about 8%.²⁷ They have been found to occur when substances with amine radicals are administered along with MAOI.^{27,28} The attacks are characterized clinically by sudden throbbing headache, flushing, hyperpyrexia, high systolic and diastolic blood pressure. Rarely cerebrovascular accidents, heart failure, and death have occurred. Many of the reported hypertensive crises have occurred with tranylcypromine, but there is no evidence that the relative incidence of attacks is greater with this drug than with other MAOI.²¹ The most common precipitating agent has been tyramine in cheese. Yeast extracts such as Marmite and Bovril contain tyramine as well as histamine and have produced hypertensive attacks. Alcoholic beverages, cream, chocolate, and broad beans have also been implicated. Presumably the hypertensive reaction occurs in patients on MAOI because tyramine and other ingested pressor amines escape oxidative deamination which would usually occur in the gut and liver. They are thus free to release norepinephrine from

nerve endings where it may²¹ or may not²⁷ be stored in supranormal amounts. Patients taking MAOI should be carefully warned against eating substances that might cause a hypertensive crisis. Hypertensive crises are best treated with a short acting alpha adrenergic blocking agent such as phentolamine, administered parenterally.^{21,27}

EKG Effects

During the past several years, predictable electrocardiographic changes have been found after administration of several psychotropic drugs. Generally these changes have involved the ST segment and the T wave, and have not been felt to be clinically significant or dangerous to the patient. This is in distinction to certain arrhythmias which have been associated with psychotropic drugs that will be discussed below.

EKG changes produced by phenothiazines have been studied primarily with thioridazine. Kelly, *et al.*,²⁹ in 1963, and Ban and St. Jean³⁰ in 1964 first reported EKG changes with thioridazine. These consisted of blunting and notching of T waves, occasional prolongation of the QT interval, increasing convexity of the ST segment, and appearance of U waves. Kelly, *et al.* suggested that thioridazine had a quinidine-like effect on the heart. Controversy arose about the significance of these changes. Wendkos³¹ performed a thorough electrocardiographic study of 50 patients on thioridazine and found that the distortion of the T wave was the only significant electrocardiographic abnormality attributable to thioridazine, and that the effect consistently occurred only when the daily dose exceeded 600 mg. He also found that, unlike quinidine induced changes, T wave abnormalities promptly disappeared with administration of a nitrate or a potassium salt. Studies by Wendkos³² and others³³⁻³⁵ have suggested that T wave changes which are reversible by potassium administration represent a benign disturbance of myocardial repolarization. A study by Alexander, Shader, and Grinspoon³⁶ on 10 patients demonstrated that it is possible from the electrocardiogram alone to determine accurately whether or not a patient is taking thioridazine. In this study, as in the study by Wedkos, the only significant abnormality noted was blunting and slight widening of the T wave which appeared at doses of 300 mg or more a day. EKG changes with chlorpromazine are less well studied in man, but animal work has documented changes similar to those found with thioridazine.

Common or predictable electrocardiographic changes with therapeutic doses of antidepressants have not been reported in the literature. Muller, *et al.*,¹⁸ studied serial electrocardiograms on 82 patients before and after treatment with imipramine. There was no evidence that imipramine had a direct effect on the electrocardiogram.

Arrhythmias and Sudden Death

Several cases of ventricular arrhythmia have occurred in association with the administration of thioridazine. Most of these arrhythmias have followed large doses of the drug. Kelly, *et al.*,²⁹ reported two fatal cases following the ingestion of 1500 and 3600 mg daily of thioridazine. It should be noted that these doses exceeded the usually recommended therapeutic range. The terminal electrocardiogram in each case showed third degree heart block with episodes of ventricular tachycardia. One case was autopsied and showed increased connective tissue and fragmented muscle fibers in the myocardium, most marked in the interventricular septum. Recently a third fatal case³⁷ has been reported of a 19 year old boy receiving 3600 mg of thioridazine, 8 mg of perphenazine, and 4 mg of trihexyphenidyl hydrochloride. He suffered an apparent cardiac arrest, was resuscitated, and subsequently died after repeated bouts of ventricular tachycardia. On autopsy the myocardium showed scattered areas of cytoplasmic fragmentation, an infiltrate of mononuclear cells, and variable loosening of intercellular connective tissue.

There have been other examples of sudden death in individuals under treatment with phenothiazines, primarily chlorpromazine.³⁸⁻⁴¹ Some have occurred in healthy young adults. A number of mechanisms of death have been proposed, including sudden fatal arrhythmias, sudden laryngospasm with asphyxiation, and instability of the autonomic nervous system. Autopsy studies of patients treated with phenothiazines have disclosed some abnormalities in the myocardium, suggesting a possible mechanism for arrhythmias. Greiner⁴² and Hollister⁴¹ have reported pigment deposition in many tissues including the myocardium. A careful pathological study by Richardson⁴⁰ found that pigmentary deposits did not differ from non-drug treated controls. However, in 12 cases who were treated with phenothiazines and died suddenly, Richardson found unusual degenerative lesions of intramyocardial arterioles. Eight of these 12 patients had abnormal electrocardiograms before death.

A number of cases of arrhythmias, often fatal, following imipramine overdosage have been reported.⁴³⁻⁴⁸ Many of the patients have been children. Arrhythmias are a common feature of imipramine intoxication, but they usually occur in combination with respiratory depression, hypotension, and low cardiac outputs. Some common electrocardiographic findings are widened QRS complexes, depressed ST segments, abnormal T waves, multifocal extrasystoles of atrial and ventricular origin and ventricular tachycardia.⁴³

Use of Psychotropic Drugs in Patients with Cardiovascular Disease

The most general concern in administering psychotropic drugs to patients with cardiovascular disease is the effect of such agents on blood pressure. Obviously the postural hypotension produced by the phenothiazines and the antidepressants is potentially more dangerous to an individual with a compromised cardiovascular status. Care should be used in administering these agents to patients with a history of syncope, transient cerebral ischemia, cerebrovascular accident, coronary artery disease, cardiac arrhythmia. Before administering antidepressants or phenothiazines to an elderly patient, the physician should consider the patient's cardiovascular status, state of hydration, electrolyte balance, and liver function. Some difficulties are often attributable to the altered patterns of elimination and absorption in the elderly. Repeated blood pressure readings, lying and standing, may be advisable during the first days of treatment to observe the magnitude of postural hypotension, particularly when the patient's cardiovascular status is in question. In elderly patients lower doses than are usually employed in younger patients may be given with a satisfactory clinical effect.

Several considerations are important in treating hypertensive patients with antidepressants. The MAOI have antihypertensive properties of their own, as discussed above. Combination of MAOI with alpha methyl dopa²¹ or rauwolfia compounds⁴⁹ can result in an agitated delirium or hypertensive reaction.

The antihypertensive action of guanethidine and related compounds is antagonized by the tricyclic antidepressants. A number of animal studies have demonstrated this antagonism.⁵⁰⁻⁵³ Recently clinical studies⁵⁴⁻⁵⁶ have shown that when desipramine or protryptiline was administered to hypertensive patients on clinically effective doses of guanethidine or bethanidine, blood pressure rose to levels that

existed prior to antihypertensive treatment. Maximum antagonism developed after twelve hours with guanethidine, and after four hours with bethanidine. Antagonism continued for five days after stopping the tricyclics. This antagonism can be explained by the hypothesis that tricyclic antidepressants block a specific transport system for amines in the neuronal membrane. Active uptake via this system is thought to be the primary mode of inactivation of norepinephrine once it is released onto the receptor site. This membrane pump is also thought to transport hydrophilic nitrogenous bases such as guanethidine to their intracellular site of action.⁵⁷ Lipophilic compounds such as reserpine do not require an active transport mechanism to cross the neuronal membrane. The antihypertensive action of reserpine is not blocked by tricyclic antidepressants.

Many psychotropic agents must be used with caution in patients with coronary artery disease. Difficult therapeutic decisions arise because many patients with heart disease suffer from depressions and anxiety states. It has recently been recognized that patients treated in intensive care units often experience acute psychoses.⁵⁸⁻⁶⁰

Tricyclic antidepressants must be used with extreme caution in patients with coronary artery disease or rheumatic heart disease and should be discontinued if there is any evidence of postural hypotension. A number of clinical reports have documented myocardial infarction or congestive heart failure occurring shortly after the initiation of treatment with imipramine.⁶¹⁻⁶⁵ Many of the cases reported had preexisting evidence of arteriosclerotic heart disease or rheumatic heart disease. In the study by Muller, *et al.*, mentioned above, two groups of individuals receiving imipramine were compared: a group of 41 individuals under 60 years of age without demonstrable cardiovascular disease, and a group of 50 patients with various degrees of generalized or coronary atherosclerosis. No serious cardiovascular side effects occurred in the group under 60 years of age. In the group with underlying cardiovascular disease, four patients developed congestive heart failure and two patients developed acute myocardial infarctions during hypotensive episodes. As mentioned earlier, postural hypotension was more common and more severe in the group with cardiovascular disease. The mechanisms responsible for these cardiac complications in humans are not clearly understood. In dogs, imipramine in doses of 2.5 mg/kg decreases myocardial contractility and cardiac output.¹⁹ It also shortens

diastole, thereby impairing cardiac filling, in dogs given doses larger than 1 mg/kg.²⁰

The MAOI relieve angina in many patients with coronary artery disease. Early reports of this phenomenon were extremely optimistic.^{66,67} One study claimed that MAOI increased exertional tolerance and caused improvement of the EKG and Master's Two-Step test in patients with coronary artery disease.⁶⁶ Later studies failed to confirm that the EKG or Master's Two-Step test improved with MAOI.⁶⁸ Furthermore the patients experienced many unpleasant autonomic side effects that led them to discontinue the medication. Many possible mechanisms for the antianginal effect of MAOI have been proposed including analgesia, CNS stimulation, ganglionic blockade, an oxygen sparing effect, and coronary dilatation.⁶⁹ A recent study⁷⁰ has demonstrated a positive correlation between mean doses of organic nitrates administered to patients for anginal pain, and the ability of the nitrate to inhibit MAO activity.

If phenothiazines are administered to patients with coronary artery disease, close attention must be paid to the development of postural hypotension. The piperazine group (e.g. trifluoperazine) is less likely to produce postural hypotension and thus may be used with a greater margin of safety. Theoretically, it could be hazardous to administer phenothiazines to a patient with an acute myocardial infarction. Clinical experience, however, has been insufficient to adequately support or negate this possibility. Recently several young patients were reported who developed congestive heart failure, myocardial infarction, or other electrocardiographic abnormalities during prolonged treatment with various combinations of antidepressants and phenothiazines. One of these patients, who had electrocardiographic evidence of an old myocardial infarction, developed an acute myocardial infarction during treatment with chlorpromazine alone.⁷¹ Confirmation of such findings is essential before any conclusions can be made.

Minor tranquilizers and barbiturates are often used in the treatment of anxiety in cardiac patients. The minor tranquilizers were not discussed earlier in this review because, when used in recommended doses, they do not have significant cardiovascular effects. In clinical practice today the choice of which antianxiety agent to use is largely made on the basis of personal preference. Certain properties of these drugs should be kept in mind when treating patients with coronary artery disease. Phenobarbital has the disadvantage of being a general CNS de-

pressant and of interfering with the anticoagulant activity of coumarin drugs by enzyme induction in the liver in susceptible patients. Recently it has seemed that the benzodiazepine group of minor tranquilizers might be more appropriate for these patients. Further investigation in this area is sorely needed. Studies are currently underway in our laboratory comparing the effects of phenobarbital, two benzodiazepines, and placebo in ambulatory patients with recent myocardial infarctions.

References

1. Bishop, M. P., Mason, L. B., and Gallant, D. M.: Blood Pressure Abnormalities in Schizophrenic Patients. *Curr. Therap. Res.* 10: 315-322, 1968.
2. National Institute of Mental Health, Psychopharmacology Service Center Collaborative Study Group: Phenothiazine Treatment in Acute Schizophrenia. *Arch. Gen. Psychiat.* 10: 246-261, 1964.
3. Bourgeois-Gavardin, M., Nowill, W. K., Margolis, G., and Stephen, C. R.: Chlorpromazine: A Laboratory and Clinical Investigation. *Anesthesiol.* 16: 829-847, 1955.
4. Foster, C. A., O'Mullane, E. J., Gaskell, P., and Churchill-Davidson, H. C.: Chlorpromazine: A Study of its Action in Man. *Lancet* 2: 614-617, 1954.
5. Crimson, C.: Chlorpromazine and Imipramine: Parallel Studies in Animals. *Psychopharm. Bull.* 4: 9-15, 1967.
6. Hollister, L. E., Caffey, E. M., and Klett, J. C.: Abnormal Symptoms, Signs, and Laboratory Tests During Treatment with Phenothiazine Derivatives. *Clin. Pharm. and Ther.* 1: 284-293, 1960.
7. Blumberg, A. G., Klein, D. F., and Pollack, M.: Effects of Chlorpromazine and Imipramine on Systolic Blood Pressure in Psychiatric Patients. Relationships to Age, Diagnosis, and Initial Blood Pressure. *J. Psychiat. Res.* 2: 51-60, 1964.
8. Sommerness, M. D., Luciro, R. J., Hamlon, J. S., and Mahowald, A. M.: Chlorpromazine, A Controlled Study with Highly Disturbed Patients. *Dis Nerv. System* 18: 16-20, 1957.
9. Koroš, B., Lang, W. J., Brown, M. L., and Gershon, S.: Effects of Chronic Chlorpromazine Administration on Systemic Arterial Pressure in Schizophrenic Patients: Relationship of Body Position to Blood Pressure. *Clin. Pharm., and Ther.* 6, (5): 587-591, 1965.
10. Sletten, I. W., Lang, W. J., Brown, M. L., Ballou, S. R., and Gershon, S.: Chronic Chlorpromazine Administration: Some Pharmacological and Psychological Effects in Man. *Clin. Pharm. and Ther.* 6 (5): 575-586, 1965.
11. Ginsburg, J., and Duff, R.: Effect of Chlorpromazine on Adrenaline Vasoconstriction in Man. *Brit. J. Pharmacol.* 11: 180-185, 1956.
12. Dasgupta, S. R., and Werner, G.: Inhibition of Hypothalamic, Medullary, and Reflex Vasomotor Responses by Chlorpromazine. *Brit. J. Pharmacol.* 9: 389-391, 1954.
13. Spector, S., Bogdanski, D. F., and Brodie, B. B.: Evidence That Chlorpromazine Exerts a Generalized Central Sympatholytic Action. *Federation Proc.* 16: 337, 1959.
14. Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M., and Koetschet, P.: Pharmacodynamic Properties of 3-chloro-10-(3'-dimethylaminopropyl) phenothiazine HCl (RP-4560). *Arch. Intern. Pharmacodyn.* 92: 305-361, 1953.
15. Friend, D. Personal communication.

16. Klerman, G. L., and Cole, J. O.: Clinical Pharmacology of Imipramine and Related Antidepressant Compounds. *Pharm. Rev.* 17 (2): 101-141, 1965.
17. Lunn, V. and Kristiansen, E. S.: Kardiale Komplikationen bei der Tofranil-Behandlung. *Wien. Med. Wschr.* 110: 754-756, 1960.
18. Muller, O. F., Goodman, N., and Bellet, S.: The Hypotensive Effect of Imipramine Hydrochloride in Patients with Cardiovascular Disease. *Clin. Pharm. and Ther.* 2: 300-310, 1961.
19. Sigg, E. B., Osborne, M., and Korol, B.: Cardiovascular Effects of Imipramine. *J. Pharmacol. Exptl. Therap.* 141: 237-243, 1963.
20. Cairncross, K. D., and Gershon, S.: A Pharmacological Basis for the Cardiovascular Complications of Imipramine Medication. *Med. J. Australia* 49: 372-375, 1962.
21. Goodman, L. S., and Gilman, A.: *The Pharmacological Basis of Therapeutics*. Macmillan Co., New York. Third Edition, 1965.
22. Maxwell, M. H., Bernstein, H., Roth, S., and Kleeman, C.: Monoamine-oxidase Inhibitors in Hypertension. *Amer. J. Cardiol.* 6: 1146-1151, 1960.
23. Harnes, J.: The Effect of Marsilid on Blood Pressure in Hypertensive Patients. *J. Clin. and Exper. Psychopath.* 19: 152-160, 1958.
24. Gillespie, L., Terry, L. L., and Sjoerdsma, A.: The Application of a MAOI, 1-phenyl-2 hydrazinepropane (JB-516) to the Treatment of Primary Hypertension. *Amer. Heart J.* 58: 1-12, 1959.
25. Oates, J. A., Seligmann, A. W., Clark, M. A., Rouseau, P. and Lee, R. E.: The Relative Efficacy of Guanethidine, Methyl dopa and Pargyline as Antihypertensive Agents. *New Eng. J. Med.* 273: 729-734, 1965.
26. Cohen, R. A.: in False Nemochemical Transmitters—NIH Clinical Staff Conference. *Ann. Int. Med.* 65: 347-362, 1966.
27. Bethune, H. C., Burrell, R. H., Culpan, R. H., and Ogg, G. J.: Vascular Crises Associated with MAOI. *Amer. J. Psychiat.*, 121: 245-248, 1964.
28. Blackwell, B., Marley, E., Price, J. and Taylor, D.: Hypertensive Interactions Between Monoamine-Oxidase Inhibitors and Food Stuffs. *Brit. J. Psychiat.*, 113: 349-365, 1967.
29. Kelly, H. G., Fay, J. E., and Laverty, S. G.: Thioridazine Hydrochloride (Mellaril): Its Effect on the Electrocardiogram and a Report of Two Fatalities with Electrocardiographic Abnormalities. *Canad. Med. Assoc. J.* 89: 546-554, 1963.
30. Bau, T. A., and St. Jean, A.: The Effect of Phenothiazines on the Electrocardiogram. *Canad. Med. Assoc. J.* 91: 537-540, 1964.
31. Wendkos, Martin H.: The Significance of Electrocardiographic Changes Produced by Thioridazine. *J. New Drugs.* 4: 322-332, 1964.
32. Wendkos, Martin H.: The Effects of a Potassium Mixture on Abnormal Cardiac Repolarization in Hospitalized Psychiatric Patients. *Amer. J. Med. Sci.* 249: 412-419, 1965.
33. Desautels, S., Filteau, C., and St. Jean, A.: Ventricular Tachycardia Associated with Administration of Thioridazine Hydrochloride (Mellaril). *Canad. Med. Assoc. J.* 90: 1030-1031, 1964.
34. Sleeper, J. C., and Orgain, E. S.: Differentiation of Benign from Pathologic T Waves in the Electrocardiogram. *Amer. J. Cardiol.* 11: 338-347, 1963.
35. Wasserburger, R. H., and Corliss, R. J.: Value of Oral Potassium Salts in Differentiation of Functional and Organic T wave Changes. *Amer. J. Cardiol.* 10: 673-687, 1962.
36. Alexander, S., Shader, R., Grinspoon, L.: Electrocardiographic Effects of Thioridazine Hydrochloride (Mellaril). *Lahey Clinic Bull.* 16: 207-215, 1967.
37. Giles, T. D. and Modlin, R. K.: Death Associated with Ventricular Arrhythmia and Thioridazine Hydrochloride. *JAMA* 205: 108-110, 1968.
38. Leestma, J. E., and Koenig, K. L.: Sudden Death and Phenothiazines. *Arch. Gen. Psychiat.* 18: 137-148, 1968.
39. Reinert, R. E., and Hermann, C. G.: Unexplained Deaths During Chlorpromazine Therapy. *J. Nerv. Ment. Dis.* 131: 435-442, 1960.
40. Richardson, H. L., Graupner, K. I., and Richardson, M. E.: Intramyocardial Lesion in Patients Dying Suddenly and Unexpectedly. *JAMA* 195: 254-260, 1966.
41. Hollister, L. E., and Kosek, J. C.: Sudden Death During Treatment with Phenothiazine Derivatives. *JAMA* 192: 1035-1038, 1965.
42. Greiner, A. C., and Nicolson, G. A.: Pigment Deposition in Viscera Associated with Prolonged Chlorpromazine Therapy. *Canad. Med. Assoc. J.* 91: 627-635, 1964.
43. Sacks, M. H., Bonforte, R. J., Lasser, R. P., and Dimich, I.: Cardiovascular Complications of Imipramine Intoxication. *JAMA* 205: 588-590, 1968.
44. Giles, H. M.: Imipramine Poisoning in Childhood. *Brit. Med. J.* 2: 844-846, 1963.
45. Rasmussen, J.: Amitriptyline and Imipramine Poisoning. *Lancet* 2: 850-851, 1965.
46. Arneson, G. A.: A Near Fatal Case of Imipramine Overdosage. *Amer. J. Psychiat.* 117: 934-936, 1961.
47. Garrison, H. F., and Moffitt, E. M.: Imipramine Hydrochloride Intoxication. *JAMA*, 179: 456-458, 1962.
48. Alajem, N., and Albagli, C.: Severe Imipramine Poisoning in an Infant. *Amer. J. Dis. Child.* 103: 702-705, 1962.
49. *Brit. Med. J.* Today's Drugs: Monoamine Oxidase Inhibitors. 2: 35, 1968.
50. Kaumann, A., Bosso, N., and Aramendia, P.: The Cardiovascular Effects of N-(γ -Methylaminopropyl-Imino-Dibenzyl)-HCl (Desmethylimipramine) and Guanethidine. *J. Pharmacol. Exp. Ther.*, 147: 54-64, 1965.
51. Stone, C. A.: Antagonism of Certain Effects of Catecholamine-Depleting Agents by Antidepressant and Related Drugs. *J. Pharmacol. Exp. Ther.* 144: 196-204, 1964.
52. Chang, C. C., Costa, E., and Brodie, B. B.: Interaction of Guanethidine with Adrenergic Neurons. *J. Pharmacol. Exp. Ther.* 147: 303-312, 1965.
53. Carlsson, A., and Waldeck, B.: Mechanism of Amine Transport in the Cell Membranes of the Adrenergic Nerves. *Acta Pharmacol.* 22: 293-300, 1965.
54. Mitchell, J. R., Arias, L., and Oates, J. A.: Antagonism of the Antihypertensive Action of Guanethidine Sulfate by Desipramine Hydrochloride. *JAMA* 202: 973-976, 1967.
55. Leishman, A. W. D., Mathews, H. L., and Smith, A. J.: Antagonism of Guanethidine by Imipramine. (Letter to the Editor). *Lancet* 1: 112, 1963.
56. Gulati, O. D.: Antagonism of Adrenergic Neuron Blockade in Hypertensive Subjects. *Clin. Pharmacol. Ther.* 7: 510-514, 1966.
57. Pettinger, W. A., Mitchell, J. R., and Oates, J. A.: Cardiovascular Effects and Toxicity of Psychotropic Drugs in Man. Preprint.
58. Kornfeld, D. S., Zinberg, S., Malm, J. R.: Psychiatric Complications of Open Heart Surgery. *N.E.J. Med.* 273: 286-292, 1965.

59. Nahum, L. H.: Madness in the Recovery Room from Open Heart Surgery. Editorial. *Conn. Med.* 29: 771-772, 1965.
60. Margolis, G. J.: Postoperative Psychosis on the Intensive Care Unit. *Comp. Psych.* 8: 227-232, 1967.
61. Freyhan, F. A.: Clinical Effectiveness of Tofranil in the Treatment of Depressive Psychoses. *Canad. Psychiat. Assoc. J.* 4 suppl.: 86-97, 1959.
62. Lehmann, H. E., Cahn, C. H., and DeVertenil, R. L.: The Treatment of Depressive Conditions with Imipramine (G-22355). *Canad. Psychiat. Assoc. J.* 3: 155-164, 1958.
63. Mann, A. M., Catterson, A. G., and MacPherson, A. S.: Toxicity of Imipramine: Report on Serious Side Effects and Massive Overdosage. *Canad. Med. Assoc. J.* 81: 23-28, 1959.
64. Malitz, S., Wilkens, B., and Esecover, H.: Preliminary Evaluation of Tofranil in a Combined In-patient and Out-patient Setting. *Canad. Psychiat. Assoc. J.* 4 suppl.: 152-159, 1959.
65. Sloman, L.: Myocardial Infarction During Imipramine Treatment of Depression. *Canad. Med. Assoc. J.* 82: 20-22, 1960.
66. Ceasarman, T.: Marsilid in the Treatment of Angina Pectoris. *J. Clin. Exptl. Psychopath.* 19, Suppl. 1: 169-177, 1958.
67. Cossio, P.: Contribution of Iproniazid to the Treatment of Angina Pectoris. *Ann. New York Acad. Sc.* 80: 1009-1015, 1959.
68. Master, A. M., and Donoso, E.: Iprinoiazid in the Anginal Syndrome Due to Coronary Disease. *Ann. New York Acad. Sc.* 80: 1020-1030, 1959.
69. Griffith, G. C.: Amine Oxidase Inhibitors, Their Current Place in the Therapy of Cardiovascular Disease. *Circ.* 22: 1156-1165, 1960.
70. Ogawa, K., and Gudbjarnason, S.: A Connection Between the Inhibition of Monoamine-oxidase Activity and the Relief of Angina Pain by Organic Nitrates. *Arch. Int. Pharmacodyn.* 172: 172-182, 1968.
71. Alexander, C. S.: Cardiotoxic Effects of Certain Psychotropic Drugs Including Electron Microscopic Changes on Myocardial Biopsy. Read at American Heart Association, November 21, 1968, Miami Beach, Florida.

Osler's Treatment Of Carcinoma Of The Stomach

In early surgical treatment lies the only hope, but there is great difficulty in the diagnosis, and it would be absurd to suggest operation in every case of dyspepsia of three months' standing in persons above forty years of age. Operated upon early, complete removal is sometimes possible. In a majority of cases the operation is only palliative. In suitable cases early exploration should be advised; the operation *per se* is sometimes beneficial and the patient is rarely the worse for it. The diet should consist of readily digested substances of all sorts. Many patients do best on milk alone. Washing out the stomach, which may be done with a soft tube without any risk, is particularly advantageous when there is obstruction at the pylorus, and is by far the most satisfactory means of combating the vomiting. The excessive fermentation is also best treated by lavage. When the pain becomes severe, particularly if it disturbs the rest at night, morphia must be given. One-eighth of a grain, combined with carbonate of soda (gr. v), bismuth (gr. v-x), usually gives prompt relief, and the dose does not always require to be increased. Creasote (m j-ij) and carbolic acid are very useful. The bleeding in gastric cancer is rarely amenable to treatment.—Osler, W.: *The Principles and Practice of Medicine*, ed 7, New York: D. Appleton & Co., 1911, p. 486.

Scintillation Scanning In A Community Hospital: A Review Part III

Chester J. Kay, M.D.

The normal thyroid photoscan may be likened to a butterfly (figure 1). The lobes are often asymmetrical. The isthmus is depicted to a variable extent depending on its thickness. A pyramidal lobe occasionally may be seen ascending from the isthmus.



Figure 1

Normal anterior thyroid scan. (photographically enlarged)

The most common indication for scanning is the evaluation of a thyroid nodule. For practical purposes a hot nodule, or one that retains more radioiodine than adjacent thyroid tissue does not represent a cancer. It may produce clinical hyperthyroidism, and may also be responsible for the suppression of iodine uptake in normal thyroid tissue.^{3,4} The latter appears as one or more cold areas on the scan (figure 2). Rescanning one day after the administration of 10 units of thyroid stimulating hormone, or after 75 to 100 micrograms of liothyronine for four to seven days should produce increased pickup in the suppressed areas and thus differentiate them from true non-functioning "cold" nodules.

DR. CHESTER J. KAY, attending radiologist at Park City Hospital, Bridgeport, and clinical instructor in radiology at the Albert Einstein College of Medicine.

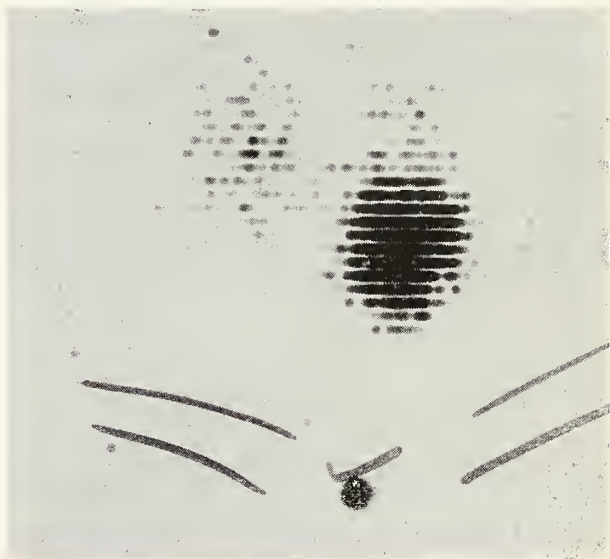


Figure 2

Autonomous hot nodule in the lower pole of the left lobe of the thyroid suppressing activity in the upper pole and right lobe.

While a single cold nodule may represent such entities as a cyst, adenoma (figure 3), inflammation, hemorrhage, or fibrosis, there is a significant risk that it represents carcinoma. Oblique projections occasionally are helpful in evaluating the presence of a cold nodule. A single cold nodule generally necessitates surgical intervention particularly if there is no pickup on a repeat scan after TSH stimulation of the gland.⁵

Scanning may be helpful in evaluating the enlarged gland. An example of a diffusely enlarged gland in a patient with Grave's disease is shown in figure 4. A multinodular goiter, in contrast, may have irregular enlargement and patchy distribution of the iodine with multiple cold areas. Cancer is much less likely in these glands.

Substernal extension is easily documented but it must be remembered that the thyroid gland moves superiorly in relation to the sternum in the normal scanning position with the neck extended, and appears lower on the conventionally positioned postero-anterior chest roentgenogram.



Figure 3

Large "cold nodule" in a substernal thyroid which proved to be an adenoma.

The differentiation of whether a mass in the neck represents functioning thyroid tissue or other structures may be made with a scan.

Congenital abnormalities such as a thyroglossal duct cyst or sublingual thyroid are depicted.

There is still disagreement as to how valuable a test of thyroid function the scan alone is. Certainly it provides information as to how each area of the gland functions in contrast to other procedures which show how the whole gland works. This can be clinically significant as in the case of a hot autonomous nodule producing hyperthyroidism with a normal radioactive iodine uptake value.



Figure 4

Grave's disease. Note diffusely enlarged gland with increased activity. Slight motion artifact is present near the upper poles.

The scan should generally be correlated with clinical history, physical examination and other parameters of thyroid function.

Pancreatic Scanning

Despite refinements of old methods and the introduction of newer radiographic techniques such as selective celiac arteriography, and duodenography, the diagnosis of carcinoma of the pancreas all too often remains elusive. This has spurred research for an isotope that can be selectively concentrated in the pancreas and one which is also technically suitable for scanning. The results have only been partially successful.

Selenium⁷⁵ can be substituted for the sulphur atom in methionine, an amino acid metabolized in the pancreas, and the resultant selenomethionine injected intravenously. This compound is picked up in both the liver and pancreas.⁶ Since the liver can hide part or all of the pancreas on a photoscan, a technique has been developed in which the liver is scanned first with radiogold and the counts over the liver electronically subtracted from the subsequent selenomethionine pancreatic scan leaving a picture of the pancreas alone⁷ (figure 5). Pickup over the spleen, kidneys and bowel may cause confusion.

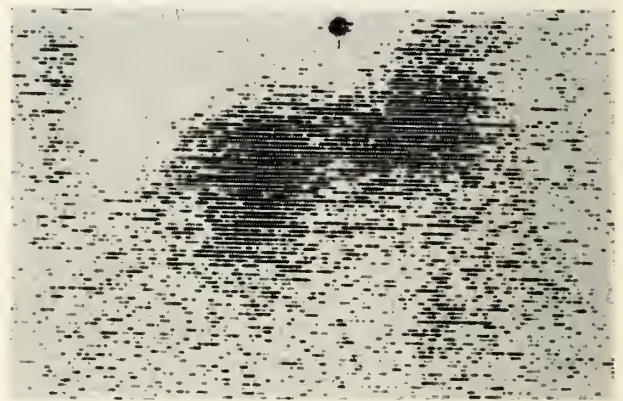


Figure 5

Normal pancreatic scan using electronic subtraction technique. The bare area in the upper left is where the liver is. Note decreased counts in the neck of the pancreas. (courtesy Dr. Arthur Hutner).

While opinions differ, it is probably not necessary to prepare the patient with a special diet. The patient is scanned in the 20 degree left anterior oblique recumbent position soon after injection.

The shape of the pancreas may vary considerably.⁸ The neck of the organ (area distal to the

head) may normally be quite thin and lead to false positives. Uncertainty about the normal variation of the tail is another common cause of error.

The gland visualizes in about 90 percent of scans. Any process that destroys parenchyma will produce a local area of decreased radioactivity. If a major duct is obstructed or the process invades extensively, the activity will be diffusely poor. Thus either a cancer or a cyst may appear as a localized cold area. The presence of pancreatitis produces a patchy appearance and if the process is active, the pancreas may not visualize at all. Inactive pancreatitis produces little or no change from normal pancreatic activity.

Both the false positive and false negative rates are significant.⁸⁻¹¹ They have varied widely from series to series. While selenomethionine enables us to scan the pancreas, it has still left a lot of room for a more satisfactory scanning material.

Parathyroid Scanning

Selenium⁷⁵ selenomethionine concentrates in areas of parathyroid hyperactivity such as adenomas,¹² but the relative concentration in the tumor compared to surrounding tissue is low. From a practical point of view, this type of scan has generally not proven to be a good screening procedure. If the diagnosis of hyperparathyroidism has been established and a surgeon is definitely planning to explore the patient for a possible parathyroid adenoma, pre-operative scanning may be helpful in localizing the tumor.

Recent reports have shown pickup of selenomethionine in lymphomas and thymomas.

Acknowledgment

Mrs. Mary Stephenson for invaluable help.

Bibliography

1. Lilly, R. L., Statistical evaluation of ¹²⁵I vs. ¹³¹I for scanning cold lesions, *J. Nuclear Med.* 5:887, 1964.
2. Andros, G., Harper, P. V., Lathrop, K., McCardle, R. J., Per technitate ^{99m}Tc localization in man with applications to thyroid scanning and study of thyroid physiology. *J. Clin. Endo.*, 25:1067, 1965.
3. Miller, J. M., and Hamburger, J. I., Thyroid Scintigram, *Radiology*, 84:66, 1954.
4. Miller, J. M., Horn, R. C., and Block, M. A., Autonomous functioning thyroid nodule in evaluation of nodular goiter, *J. Clin. Endo.*, 27:1264, 1967.
5. Gibbs, Jr., J. C., Halligan, E. J., Grieco, R. V. and McKeown, J. E., Scintiscanning the thyroid nodule: Aid in its surgical management, *Arch. Surg.*, 90:323, 1965.
6. Blabe, M. and Manske, R. F., The pancreas specificity of Se⁷⁵ selenomethionine. *J. Nuclear Med.*, 2:102, 1961.
7. Eaton, S. B., Potsaid, M. S., Lo, H. H., and Beaulieu, E., Radioisotope "Subtraction" scanning for pancreatic lesions. *Radiology*, 89:1033, 1967.
8. Riccobono, X. J., Pancreatic scanning, *Sem. in roent.* 3:310, 1968.
9. Burdine, J. A. and Haynie, T. P., Diagnosis of pancreatic carcinoma by photoscanning, *J.A.M.A.*, 194:979, 1965.
10. Sodec, D. B., Pancreatic scanning. *Radiology*, 87:641, 1966.
11. Rodriquez-Antúnez, A., Filson, E. J., Sullivan, B. H., Jr., and Brown, C. H., Photoscanning in diagnosis of carcinoma of the pancreas. *Ann. Int. Med.* 65:730, 1966.
12. Potchen, E. J., Watts, H. G., and Awwad, H. K., Parathyroid scintiscanning, *Rad. Clin. N. A.*, 5:267, 1967.

Freud On Bisexuality

We are faced with the great enigma of the biological fact of the duality of the sexes. It is an ultimate fact of our knowledge, it defies every attempt to trace it back to something else. . . . Psychoanalysis has contributed nothing to clearing up this problem which clearly falls within the province of biology. In mental life we can only find reflections of this great antithesis, and their interpretation is made more difficult by the fact, long suspected, that no individual is limited in modes of action to a single sex but always finds some room for those of the opposite. . . . We call everything that is strong and active male and everything that is weak and passive female. The fact of psychological bisexuality embarrasses all our inquiries into the subject.

The Role of the Community Hospital In Patient Care And Medical Education

Leon Gordis, M.D.

In recent years there has been increasing awareness of the disparity between the type of training a physician receives during his residency and the problems and challenges he meets when he enters practice. There has been strong feeling that training a physician in the esoteric most of the time is not an adequate way to equip him for many of the services he is called upon to render in the reality of the outside world beyond the hospital walls. There has, therefore, developed the concept of community medicine which has been expounded with great clarity by Haggerty¹ as reflecting a new concern with all the medical needs of the patient coming for care, resulting in an orientation to the patient rather than to a specific disease with which he presents. Furthermore, it is distinguished from comprehensive medicine in that it extends to a concern for the health needs of all people in the community, not only for those who seek medical attention. Although this concept in large measure may not be new, what is perhaps new is its increasing acceptance by both university and non-university hospitals which are facing up to the problem of how one teaches this type of approach.

Perhaps one of the most pressing needs in the teaching of community medicine is to convey to our young physicians the need for looking at patients as patients and not merely as bearers of a disease which is of medical interest. All too often the patient with an interesting illness becomes the victim rather than the beneficiary of our medical care system. This can be vividly demonstrated in a letter received at Johns Hopkins from a distraught mother who wrote as follows:

"Please, can you advise us as to how we can help the boy, what we can do for him at home, how much you charge to see him, and what is available in the way of educational facilities for such a child from a lower income family?

Also, when could you see him?

Ever since they figured out the name of what's wrong with him here, a pretty ridiculous situation has arisen. The psychologists, doctors, teachers, etc., that work with various types of handicapped children all want to get a look at him, like he's the eighth wonder of the world.

They wonder, marvel, shake their heads and it usually ends up with me telling them what receptive expressive aphasia is and how it affects the child, which is, as I said, rather ridiculous when you consider that I'm paying them to tell me what to do for him.

I sent away through the book store for this book "The Care and Habilitation of the Aphasic Child" it costs \$24.00 but it's the only thing that makes any sense in helping him that I've come across and I've hounded the College libraries here.

Before I forget, he scores fifty in a standard Binet test.

His hearing is supposed to be normal with the tuning fork bit so they didn't bother with the galvanometer thing.

He's had all sorts of tests. Some were so bad I'm never going to let anybody do again. He had EEG and the one where they put air in his spinal cord and he had dye in the artery going to the brain and they put holes in his skull and then put dye in them.

When it was all through they say receptive expressive aphasia. When he was fourteen months old I figured out what is wrong only I didn't know there was a name for it as that anybody else ever had it. I used to say he could hear but that for some reason words didn't have any meaning for him.

They tell me you understand about children like him at your hospital and that you know how to habilitate them. If that's so, then you are the people I want for him. If you really aren't, please tell me now.

DR. LEON GORDIS, Chief, Department of Community Medicine, Sinai Hospital of Baltimore, and Assistant Professor of Pediatrics, Johns Hopkins School of Medicine.

Presented to the Department of Pediatrics, Hartford Hospital, February 21, 1969.

I don't want to drag him all the way to Baltimore to tell you what's wrong with him and why. I only went through high school. I don't understand that much about lesions or convulsions and all that stuff.

If I sound half crazy, it's probably because I am, from worrying how to get help for this kid. Thank you for any help you can give us."

This poignant letter points up many of the qualities that must be built into the practice of medicine today. It is quite clear that the child's condition and its serious impact on his family and community have gone totally unappreciated by the professionals in the different institutions which the family consulted. Our younger men must therefore be taught not only the sensitivity necessary in handling chronic problems of this sort but also the need for integration and coordination of services and long-term planning of health care needs. However, the teaching of community medicine must stress not only continuity and comprehensiveness of care, sensitivity of care, and appreciation of a disease in its social context, but must also be integrally linked with teaching and research, primarily medical care research, or the evaluation of the organization of the system in which we provide the care. With this point of view, therefore, there is a need for teaching a body of methodology and didactic information, including biostatistics, epidemiology, and research design.

However, the role of the community hospital in training men in community medicine is becoming increasingly complex. For years, community medicine was, in essence, the private domain of the community hospital. University medical centers displayed little, if any, interest in this area from either the care or the research standpoint. Government agencies virtually pleaded with community hospitals to submit grants for service and research problems in this area. However, times have changed in terms of federal financing, and in large measure the pendulum has swung from subsidization of basic research to increasing emphasis on research and care in the community area. With this shift in the pendulum, there has also come about a concomitant shift in the orientation of university medical centers. These institutions are now becoming increasingly active in the community area, whether because of a profound change in convictions or because of a recognition of the new financial realities of our day. In any event, the fact is that community hospitals no longer have a monopoly on virtue

and find themselves directly in competition with university hospitals for staffing and financing in the area of health care and health care research.

This change in affairs has necessitated a painful reexamination by the community hospital of what unique role, if any, it has both in provision of medical care and in the training of young physicians. One may ask why the community hospital should not abdicate its present role entirely to the large university medical center? This extremely important question must be approached by examining a number of pertinent factors.

Role of the Community Hospital

There is, first of all, no doubt that community hospitals maintain their importance partially by virtue of the number of patients served, both in ambulatory and in-patient areas. By their location they are more convenient to large parts of the population and their services can be more useful on an ongoing day-to-day basis. Furthermore, they are also important in terms of the number of physicians they train. From the quantitative standpoint alone, a large part of pediatric training today is accounted for by community hospitals. In Connecticut, for example, almost half the residency positions in pediatrics are in community hospitals. University medical centers cannot provide sufficient physicians for the country and, indeed, even considering all hospitals, the output of physicians is inadequate to the health needs of the nation as a whole.²

Perhaps even more important than these factors, however, is the fact that the community hospital can easily maintain a close relationship to its community and to the practicing physicians who provide medical care in it. Traditionally, the community hospital has received its support from the community it serves and can, therefore, be particularly sensitive and responsive to the needs of that community. It is able to modify its care and to respond to emerging needs with greater facility than a large monolithic medical center. Furthermore, the community hospital is able to maintain a close working relationship with the practicing physician, not only in terms of bed privileges but in terms of policy and in terms of postgraduate education in the years after his residency training. As new developments emerge in the biologic, therapeutic, sociologic and public health areas, the community hospital can serve as a vehicle for disseminating this information and for including the

practicing physician, not only in its educational programs, but equally as important, in its developing medical care and research programs.

A further vital qualification of the community hospital is the fact that because of its administrative structure and its closeness to its community, this type of hospital is able to make more rapid progress in terms of health care innovations than larger institutions. In a community hospital, interdepartmental collaboration is frequently greatly facilitated compared with university medical centers. The greater flexibility of community hospitals should be utilized to the fullest as they plan and develop their programs.

An equally important characteristic of the community hospital is that it does not emphasize sub-specialties. The tendency of community hospitals to approach patients as generalists would, provides a better model of patient care for education of interns and residents. The *raison d'être* of a community hospital is service while that of the university medical center is often research and training. While the latter two components are vital, prime dedication to service leaves its imprint on the type of training provided by the institution. Thus, keeping in tune with the times, as health needs of the community emerge and evolve, the community hospital is able to plan and implement the specific types of services necessary to deal with them.

Community Hospital Programs

Some examples of how one community hospital has responded to newly recognized community health needs can be seen in the ambulatory care programs of Sinai Hospital in Baltimore. Seven years ago the realization that elderly patients were inadequately cared for in the community led to the establishment of an Aging Center at Sinai.³ This center which has now expanded to include chronically ill adults of all ages, provides continuous medical care from the same physician as well as round the clock coverage, weekends and nights, for a group of over 700 patients in the community. In this program, physicians are salaried on a part-time basis and the remainder of their time is spent in private practice. Not only is this a vital link in health care but it provides an important bridge between the private practicing physician and the community hospital. An adjunct to this program has been an active Home Care Program for adults which, at the present time, is the only hospital-based home care program in the State of Maryland.

A parallel program of continuous and comprehensive care for chronically ill children has also been developed in the Family Pediatric Clinic.⁴ This program was established over four years ago at Sinai Hospital to provide service to chronically ill children and to all their healthy siblings. Staffed by a health team of physician, nurse, social worker, clinical psychologist, and other professionals, the program emphasizes primary and secondary prevention and continuous management of the disease in the context of the family and the community.

One of the most noteworthy features of this program has been the opportunity it provides for the training of house staff in Community Medicine. Primary clinical care in this program is provided by the Chief Pediatric Resident, who over a period of months has the opportunity to develop his own hospital-based practice. He provides continuity of care, is available nights and weekends, and also makes house calls when indicated. In this way he learns to appreciate the importance of the social and family environment in the successful management of the chronically ill child and his family. In addition, he has the opportunity to work with a public health nurse, social worker, and other personnel, as part of a health team so that his residency experience is enriched by his participating in new patterns of providing medical care.

A more recent extension of that program is the Family Obstetrical Clinic. Recognizing the tragic fact that each year in Baltimore over 1,000 live births occur in girls 16 years of age and under, this program provides comprehensive prenatal care as well as delivery and postpartum care for pregnant adolescents. More recently, the recognition that even the most dedicated service cannot return to normalcy a girl who has had her first baby, has led to the establishment of the Adolescent Family Life Service⁵ at Sinai in which we are now providing birth control information and services to nulliparous, sexually active adolescents. These programs have been operating for the past two years and are part of an all-inclusive Adolescent Center which Sinai established and which provides care for a broad spectrum of adolescent medical, obstetrical, and behavioral problems in a single program. The clinic also provides valuable opportunities for training pediatric and obstetrical residents who rotate through the programs. This clinic meets evenings in our Outpatient Department, utilizing valuable space that is otherwise not used and coming at a time most convenient both for the patients and their families.

Regional Planning

These programs demonstrate the type of flexibility and willingness to innovate which are perhaps the unique role of the community hospital. At the same time, however, it must be recognized that the community hospital does not exist in a vacuum. Indeed, it is even less isolated now than in past years, since regionalization of medical care is almost certainly to become a reality. The Regional Medical Program has as one of its prime objectives, collaborative arrangements between medical and health institutions in given areas. It will no longer be the prerogative of any single institution to plan in isolation; planning will involve cooperative ventures in which the needs of the community are the determinant rather than the convenience of the hospital. Furthermore, in view of the problems of staff recruitment, it seems likely that only through joint endeavors with university based institutions will community hospitals be able to face the continually increasing challenge of difficulty in recruiting staff. It seems likely that programs of staff rotations and combined internships or of joint appointments between community and university hospitals will be essential and that programs of combined academic and community hospital training will have to continually evolve. However, the relationship between community hospital and university must be bilaterally beneficial and in an atmosphere of mutual respect. Furthermore, the relationship must be dynamic and evolving because the problems with which it will cope are also changing. There must be no rigidity or inflexibility nor must there be any note of condescension as university and community hospitals come to agreement in terms of training and medical care patterns.

It is also essential that the community hospital maintain its perspective and recognize that it cannot be an all inclusive empire necessarily providing every type of service. The costs of medical care are too great to permit unnecessary duplication of services. An interesting study was completed within the past several years by Crocetti⁶ who surveyed 7,000 hospitals in the United States concerning cardiac catheterization and angiocardiography laboratories as well as open and closed cardiac surgical facilities. She found that in 1961 there were 540 cardiac catheterization laboratories in the United States. Eighteen percent had not done a single procedure during the previous year. Almost 700 angiocardiography laboratories existed, but

one-third had not done a single procedure. In addition, many of those laboratories which reported that they were active had done very few procedures during the year in question. These findings raise questions not only about the extent of utilization of these resources but also about the quality of the diagnostic and therapeutic care provided when utilization is so low. This study points up the necessity for overall planning in establishing medical care facilities which must go beyond the needs of a single institution. We can no longer afford the luxury of permitting Hospital Ladies Auxiliaries or Public Relations Departments to decide which medical care facilities are needed in the community.

Ethnic and Economic Boundaries

The community hospital also has a vital role to play in another emerging long-term health problem in the United States. The great concern in recent years over the inadequacy of medical care provided to the poor, has resulted in intensive efforts at establishing comprehensive health programs in inner-city areas. Although the intentions are good and the quality of care often excellent, there exists the important hazard that in the process we are establishing two classes of health care—one for the poor and the black, and the other for middle and upper class whites. One wonders whether the doctrine of separate but equal will be any more applicable in the health care area than in the area of public education. We are reminded of the days when city housing projects were constructed which, at the time, appeared to be major improvements over the slums they were replacing but which, over the years, have resulted in an intensification of ghetto conditions and a new form of slum on their own.

In view of these considerations there is a need for ethnic and socioeconomic mixing of patients in health care programs. Such mixing is also essential if our house staff is to experience the challenge of dealing with health care problems in different cultural and socioeconomic groups. The community hospital with its clinics and its private practicing medical staff, has the potential for developing health care programs which will span racial and economic boundaries. In this area lies one of the greatest challenges to the community hospital.

In conclusion, the community hospital must utilize its own unique assets but, at the same time, must recognize that it can no longer function as a self-contained unit. Only in this way will it be able

to meet successfully its community responsibility and the challenges of the coming decades.

References

1. Haggerty, R. M., *Community Pediatrics*, New Engl. J. Med., 278: 15, 1968.
2. Knowles, J. H., *The Quantity and Quality of Medical Manpower: A Review of Medicine's Current Efforts*, J. Med. Ed., 44: 81, 1969.
3. Furstenberg, F. F., *Comprehensive Care for the Aging in the Outpatient Department*, Bull. N.Y. Acad. Med., 41: 98, 1965.
4. Markowitz, M., and Gordis, L., *A Family Pediatric Clinic at a Community Hospital*, Children, 44: 25, 1967.
5. Gordis, L., Fassett, J. D., Finkelstein, R., and Tayback, M., *Adolescent Pregnancy: A Hospital-Based Program for Primary Prevention*, Am. J. Pub. Health, 58: 849, 1968.
6. Crocetti, A., *Cardiac, Diagnostic and Surgical Facilities in the United States*, Pub. Health Rep., 80: 1035, 1965.

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Hemorrhage In Diverticulosis Of The Colon

Gioacchino S. Parrella, M.D. and C. J. Lipkoff, M.D.

Hemorrhage In Diverticulosis Of The Colon

Colonic Diverticulosis occurs in only 5% of people over 40 but the incidence increases rapidly to 33 $\frac{1}{3}$ % in the group over 50 years of age, and to 66 $\frac{2}{3}$ % of all people over 85.³ Colonic diverticula are being diagnosed in increasing numbers of patients in our hospitals and, as our aging populace increases, complications such as perforation, obstruction, or hemorrhage are more common. In 1953 Cate first recommended resection for diverticular bleeding,⁵ but there is still reluctance on the part of surgeons to accept diverticulosis as a major cause of massive hemorrhage from the bowel, and to recognize that frequently resection is required.

In massive colonic hemorrhage the exact site of bleeding is difficult to determine. Richmond and Payson,⁴ among others, have maintained that the segmental isolation of the colon at the operating table accurately localizes the hemorrhage site. With the use of a sterile sigmoidoscope and at least two colotomy incisions they were able to observe the bleeding site in a 70 year old patient who had recurrent hemorrhage and syncope. Their success in localizing the site of hemorrhage has not been universally duplicated, for even in the resected specimen the pathologist has been hard put to localize the exact area of ulceration and hemorrhage.

In an effort to study the problem more accurately, Noer² injected segments of involved colon with latex. This technique demonstrated the abnormally large number of vessels present in the walls of the diverticula and also proved, to his satisfaction, that bleeding must usually be associated with some degree of diverticulitis even though the extent of that diverticulitis may be microscopic.

Early,¹ in 1959 studied the incidence of diverticulosis and hemorrhage at the University of Virginia and found that about 41 $\frac{1}{2}$ % of the cases bled massively and repeatedly. Preoperatively diverticulitis was diagnosed by x-ray in $\frac{1}{3}$ of the cases. He concluded that cure results only when all colon

segments containing diverticula are resected, unless the surgeon is fortunate enough to demonstrate the bleeding point. In moribund patients, proximal ileostomy or colostomy was recommended.

Milford Hospital is a small community hospital of 110 beds which admits approximately 5500 patients a year. During the course of a year about 2200 operations are performed. A recent review of the problem of diverticulosis and diverticulitis at this hospital has revealed a varied experience with the problem of hemorrhage in patients with diverticulosis.

REPORT OF PATIENTS:

1. N. H., an 89 year old female, was admitted exsanguinated and dyspneic following massive hemorrhage at home. In addition to severe arteriosclerotic cardiovascular disease, x-ray examination revealed diverticulosis of the descending and sigmoid colon and the bleeding was presumed to be from the left colon. The patient received oxygen, 2000 m.l. of blood, diet therapy and a stool softener. There has been no further bleeding in a followup of two years.

2. P. S. a 78 year old male was admitted in congestive heart failure following an episode of bright red bloody rectal discharge at home. The patient had had an episode of bleeding one month prior to admission. X-ray diagnostic workup revealed arteriosclerotic cardiovascular disease, cholelithiasis, diverticulosis of the hepatic flexure and sigmoid diverticulitis. The patient was treated with oxygen, digitalis, Mercurhydrin and a transfusion of 1000 m.l. of blood over a period of several days. He refused operation and was re-admitted four months later with a third episode of bleeding. Again he refused operation and went home where he died with recurrent hemorrhage.

3. F. B. a 60 year old male suffered from mild emphysema and Parkinsonism sustained a massive rectal hemorrhage of bright red blood requiring transfusions 13 years before admission. He was admitted to Milford Hospital severely exsanguinated, and was transfused with 3500 m.l. of blood. X-ray diagnosis was diverticulosis of the left colon and diverticulitis of the sigmoid. The patient was re-admitted 6 weeks later for an elective resection of

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the left colon. There has been no further bleeding for the past two years.

4. F. W. a 71 year old female who had frequent mild episodes of rectal bleeding at home was admitted with a ventral hernia, emphysema, and arteriosclerotic cardiovascular disease. X-rays revealed diverticulosis and diverticulitis of the sigmoid. The patient was treated with a low residue diet. She was discharged on the 12th day and has not bled for the past year.

5. M. G. a 56 year old female had rectal bleeding for one month prior to admission. She was admitted for transfusions. Diverticulosis of the sigmoid was diagnosed by x-ray. She was temporarily discharged, but had to be re-admitted because of recurrent hemorrhage. A left colectomy revealed diverticulosis and diverticulitis of the colon. There has been no bleeding in a three year followup.

6. H. W. a 54 year old male had rectal bleeding 8 years before the present admission. On admission, study of this patient revealed a hiatus hernia, question of a duodenal ulcer, and evidence of an old myocardial infarct by electrocardiography study. X-rays revealed diverticulosis of the colon, mainly left sided. After four more episodes of bleeding he was admitted for resection. The resected specimen revealed diverticulitis of the left colon. There has been no further bleeding for two and a half years.

7. A. R. a 46 year old male was admitted with a massive rectal hemorrhage requiring repeated transfusions. After 72 hours of continuous bleeding he was explored. X-ray diagnosis had revealed diverticulosis sparing only the distal sigmoid and right colon. At operation diverticulosis was found to involve the entire colon and because of the surgeon's inability to pinpoint the site of hemorrhage, a colostomy was performed. A near-total colectomy with ileoproctostomy was performed at a later operation. Bleeding has not recurred.

8. J. W. a 74 year old male was admitted with a diagnosis of cirrhosis of the liver, obesity, hypertension, arteriosclerotic cardiovascular disease with old myocardial infarcts, and an amputation of the right leg due to a ruptured popliteal artery aneurysm six months prior to admission. He gave a history of having had bright red blood from the rectum three years before admission. X-ray revealed diverticulosis of the descending colon and sigmoid. He continued to bleed six days after admission despite transfusions of 1000 m.l. of blood. The left colon was resected at an emergency operation, and the resected specimen showed diverticulitis involving 63cms. of the colon. This patient expired a

year later due to a new myocardial infarction. There had been no further bleeding prior to death.

9. E. W. a 70 year old female was admitted with a medical history of arteriosclerotic cardiovascular disease with hypertension. Her past history revealed that she had had bright red blood from the rectum of significant amounts 10 years, 3 weeks and one week before admission to the hospital. X-ray examination showed diverticulosis of the left colon and diverticulitis of the sigmoid. A left colectomy was done and the resected specimen revealed diverticulosis. There has been no recurrence of hemorrhage during a five year followup.

10. J. R. a 62 year old female was admitted with arteriosclerotic cardiovascular disease, moderate cardiac decompensation duodenal ulcer, and deep thrombophlebitis of the right extremity. She gave a history of having had currant jelly blood appear from the rectum one year and a few weeks before admission to the hospital. X-ray examination showed scattered diverticula throughout the entire colon. At operation a gastrostomy was done and no upper gastrointestinal hemorrhage was demonstrated. The blood appeared to be localized in the right side of the colon and a right colectomy was done. The specimen contained diverticula and fresh blood. Because of the recent history of the deep thrombophlebitis a bilateral superficial femoral vein ligation was also performed. The patient recovered following a stormy postoperative course. Several months later the patient was seen for a mild secondary anemia with guaiac positive stools, but no evidence of fresh blood in the stools. She is alive and well four years later without recurrent severe rectal bleeding.

Discussion

Most of the patients reported here suffered from other severe complicating diseases which often mitigated against immediate operation. However, as in massive hemorrhage of the upper gastrointestinal tract, the persistence of bleeding or the recurrence of bleeding while under observation in the hospital carries with it a serious prognosis and makes emergency operation necessary. It is felt that in all such patients attempt should be made to restore the blood volume as closely as possible to normal, to treat heart failure and other complicating diseases, and to prepare the bowel with antibiotics or poorly absorbed Sulfonamide preparations.

Proctoscopy in all of these patients was of help in only a negative way since in each of them blood

was coming from above the reach of the sigmoidoscope and there was no primary lesion within the rectal ampulla.

X-ray studies help in making the diagnosis but unfortunately do not adequately demonstrate the extent of the disease nor the presence or absence of inflammatory changes within the diverticula. Even though the x-ray diagnosis is diverticulosis the resected specimen often shows inflammatory changes within the mesentery and the pathological diagnosis is almost always diverticulitis when hemorrhage is present. Even though one cannot feel an inflammatory mass, the hemorrhage must be secondary to microscopic areas of inflammatory ulceration into the rich vascular network which has been demonstrated by Noer and others.

In the overwhelming majority of patients resection of the sigmoid and left colon, (mobilizing the splenic flexure) will remove the site of the hemorrhage. In the occasional patient where there is a large amount of blood in the right colon and extensive diverticulosis involving the entire bowel, one may be forced to do a temporary transverse colostomy in order to try to localize the source of hemorrhage. The use of the sigmoidoscope through colotomy incisions at operation promises more than it delivers in practical help.

Summary

The surgeon faced with a massive colonic hemorrhage must utilize non-operative support prior to any operative procedure, and the latter individ-

ualized depending on the findings at operation and the general condition of the patient. Preoperative proctoscopy and barium enema can often be misleading and give information only in a general manner since they do not localize the source of the hemorrhage. Despite the inability to propose a definitive operation for massive colonic hemorrhage and diverticulosis, the authors are convinced that hemorrhage from the large bowel can be persistent, recurrent under conservative management, and sometimes fatal. There is no doubt that there are a few patients in whom surgical therapy initially must be the treatment of choice if one is to save the patient's life. It would appear that this type of patient will become more common in the general hospital and nursing home during the coming years as life span is increased.

References

1. Early, C. M.: The Management of Massive Hemorrhage for Diverticular disease of the colon, *Surgery, Gynecology and Obstetrics*, Vol. 108, 49-60, January 1959.
2. Noer, R. J.: Hemorrhage as a Complication of Diverticulitis, *Annals of Surgery*, Vol. 153, 851-860, June 1961.
3. Quinn, W. C.: Gross Hemorrhage from presumed diverticular disease of colon, *Annals of Surgery*, Vol. 153, 851-860, June 1961.
4. Richman, H. and Payson, B. A.: Segmental Isolation for Massive Colonic Hemorrhage, *Archives of Surgery*, Vol. 92, 107-108, January 1966.
5. Rosenbery, I. K. and Rosenberg, V. F.: Massive Hemorrhage from Diverticula of the Colon with Demonstration of the Source of Bleeding, *Annals of Surgery*, Volume 159, 570-573, April 1964.

On The Blood's Circulation

But it is certainly mysterious and incongruous that blood should be supposed to be most commodiously drawn through a set of obscure or invisible ducts, and air through perfectly open passages, at one and the same moment. And why, I ask, is recourse had to secret and invisible porosities, to uncertain and obscure channels, to explain the passage of the blood into the left ventricle, when there is so open a way through the pulmonary veins? I own it has always appeared extraordinary to me that they should have chosen to make, or rather to imagine, a way through the thick, hard, dense, and most compact septum of the heart, rather than take that by the open pulmonary vein, or even through the lax, soft and spongy substance of the lungs at large.—Harvey, William: "An Anatomical Disquisition on the Motion of the Heart and Blood in Animals," in *Classics of Medicine and Surgery*, New York: Dover Publications, Inc. (1959), p. 42.

THE PRESIDENT'S PAGE

The practicing physicians of this country have been deluged and perplexed by the seemingly endless national medical legislation enacted during the past two decades. While some measures have been constructive in nature, many have proved to be detrimental to the accepted and traditional methods of medical practice. What is even more alarming is that the end of disparaging and maligning the nation's practicing physicians is not in sight. The Society has made repeated attempts to keep you informed of legislative and program developments at the state as well as the national level, and of the stands that have been taken on behalf of its members.

Recently, the Council made *two* additional thrusts which hopefully will prove to be of importance and benefit to all Connecticut practitioners.

A delegation of nine, headed by Doctor Bernard A. Burnham, Chairman of our Committee on National Legislation, travelled to Washington, D.C. and interviewed all but Senators Ribicoff and Dodd of the eight Connecticut members of Congress. Briefly, the Representatives were engaged in discussions of a number of legislative matters and their responses accordingly evaluated. A full report of this interview will be presented to the Council and published in *Connecticut Medicine* in the near future.

Of special note:

1. An offer was made of the resources of our Society for research, advice and policy formation in regard to any proposed health legislation.

2. A request was made of all interviewed for their support in restoring the appropriation for medical student scholarship funds.

3. A plea was made for insistence that any innovations made in the delivery of health care be known to be more efficient, if not more economical, than the present system of private practice.

4. A plea was made for Congressional recognition of two factors:

a. Optimum health care must include preventive care as well as therapeutic.

b. If the best possible medical care is desired, it must be paid for, as for any other quality service.

The legislators were keenly interested in our successful experience with the welfare patient and the "usual and customary" method of reimbursement. Some have suggested that we give it national prominence through the news media.

A second important activity was the participation of four members of our Society in the regional meeting of the Council on Legislative Activities of the AMA. This full day session was held in Boston on September 20th and proved to be both informative and instructive. The agenda was extremely lengthy and only its highlights can be touched upon here.

Some of the more significant subjects covered were:

- Actions of the Board of Trustees pertaining to Legislative Activities.
- Excerpts from Actions of the House of Delegates at their meeting in New York City in July, 1969.
- Testimony on legal matters.
- Report by the AMA Lobbyist, Mr. James Forrestal.
- A commentary from the AMA Auxiliary.
- Report from the Health Insurance Benefits Advisory Council (HIBAC).
- Report from the Task Force on Medicaid and Related Programs.

This presentation, made by Doctor H. Phillip Hampton of Florida, was extremely informative, far reaching in its impact, and probably, in my opinion, the single item of most significance made by the AMA Board of Trustees in the past few years. The report was based on an electronic and computer program employed in the physician's office. The plan was referred to as "the fourth party." It apparently is to benefit the practitioners of medicine. Frankly, it resembles, in many aspects, the efforts of CUPISS. It is designed to save time and energy in the physicians' office as well as serve as a repository for data on patients for future use.

• Other items discussed: A Student Nursing Program; Alcoholism and the National Institute of Mental Health Program; AMA-sponsored legislation, and the status of selected pending legislation. With respect to the latter, emphasis was placed on a bill concerning the Hill Burton Act, the Library, Vaccination Bill, and Graduates of Foreign Medical Schools who come to this country for instruction. Reference was also made to Senator Ribicoff's proposed "Council in the White House Correlating Health Agencies."

Perhaps the item that received the most discussion was the bill proposed by the AMA "to provide for medical and hospital care through a system of voluntary health insurance financed in whole or part by income tax credits." The top-limit expenditure for such a bill was given as approximately \$7.6 billions/year. After a lengthy, and at times heated, discussion it was obvious to all concerned, including the Chairman of the session, that while the intent of the bill was clearly well-conceived and desirable, many details have yet to be worked out with the aid of insurance carriers to finalize a desirable and fair program. Thanks to our President-Elect, Dr. Morris A. Granoff, emphasis was placed on the probable impact of such a plan on not only insurance companies and physicians, but also on the public-at-large.

Stevens J. Martin, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

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CALL

SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1969 Semi-Annual Meeting of the House of Delegates will be held at the New Haven Medical Association Building, 364 Whitney Avenue, New Haven, commencing at 2:00 o'clock in the afternoon of Thursday, December 11.

Stevens J. Martin, President
Kenneth F. Brandon, Speaker of the House
Reginald C. Edson, Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12 Par. 3 of the By-laws provide that:

All resolutions to be considered as regular business at any regular meeting of the House of Delegates must be in the hands of the Speaker not later than seventy-two hours before the opening of that meeting. All resolutions and recommendations published in the official agenda distributed to the members of the House prior to the meeting at which action is to be taken shall be considered as regular business. Resolutions presented later than seventy-two hours before the opening of a meeting will be referred for consideration as regular business by the House only when they are presented by the Council or accepted for consideration by majority vote of the delegates present. Any resolution which does not qualify in accordance with the aforesaid provisions for consideration as regular business may be accepted for action by a majority vote of the delegates present and, if so accepted, shall be referred at once by the Speaker to a reference committee. Any such reference committee shall consider resolutions referred to it and shall report, with recommendations to the House before adjournment of the meeting.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the By-laws were introduced at the House of Delegates on May 14, 1969 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments will be published in Connecticut Medicine, "on one or more occasions prior to the next meeting . . . at which meeting the amendments shall be taken off the table and acted upon by the House of Delegates."

I. Vice-Chairman of the Council

Purpose: To establish the office of Vice-Chairman of the Council and define the duties thereof.

AMENDMENT

Article VII—The Council

Section 1. Powers and Duties

Paragraph 2. Chairman—Delete the entire paragraph and substitute the following.

Paragraph 2. Chairman and Vice Chairman. The Council shall annually elect from its membership a Chairman and Vice-Chairman.

The Chairman shall preside at all regular and special meetings of the Council and shall perform such duties as custom and parliamentary usage require. He may address the Council at the opening of any meeting of the Council, limiting his remarks to matters of conduct and procedure in the Council. He shall have full voting rights in the Council.

The Vice-Chairman shall aid and assist the Chairman and shall officiate for the Chairman during his absence or at his request. In the case of death, resignation or removal of the Chairman, the Vice-Chairman shall immediately become Chairman and shall serve the remainder of the term of his immediate predecessor. He shall have full voting rights in the Council.

In the absence of both the Chairman and Vice-Chairman, the President shall preside.

II. The Judicial Committee

Purpose: To make it mandatory for the Judicial Committee to file a report at each annual meeting of the House of Delegates.

AMENDMENT

(Add the underlined words)

Article X. Committees of the Council

Section 3. Judicial Committee

Paragraph c. (5) The Judicial Committee shall render a semi-annual report to the Council including its actions, opinions, and recommendations and shall make such interim reports as it desires or as are requested by the Council. Such reports shall be available to members of CSMS.

The Committee shall also file a report of its activities at each annual meeting of the House of Delegates.

III. The Judicial Committee

Purpose: To require the endorsement of the House of Delegates on any "rule of ethics" recommended by the Judicial Committee before it becomes binding upon all members of the Society.

AMENDMENT

(Add the underlined words)

Article X. Committees of the Council

Section 3. Judicial Committee

Paragraph c(I) . . . Its (the Judicial Committee's) decisions shall be binding on the parties concerned and specific problem considered, but shall be considered only as a presumption of the Society, binding on all members only when endorsed by the Council and the House of Delegates and published by the Society to the membership.

IV. Committee on Medical Care of Veterans

Purpose: To abolish the Committee on Medical Care of Veterans and transfer its duties to the Committee on Third Party Payments.

AMENDMENT

Article XI. Divisional Boards and Committees

Section 3. Divisional Standing Committees

Paragraph c. Medical Economics Division

Delete the words "Committee on Medical Care of Veterans"

Section 5. Duties of Standing Committee

Paragraph 10. Committee on Medical Care of Veterans. (Delete in its entirety.) Renumber paragraphs 10 through 28

Paragraph 12. Committee on Third Party Payments. (Delete underlined words.) . . . In its opera-

tions, the committee shall confer directly with agencies which have an interest and responsibility in systems that involve payment of physicians by third party agencies but, where other standing committees of The Society have direct relationships, such as the Committee on Medical Care of Veterans, the committee shall confer with such other standing committees rather than directly with the agencies involved.

V. Committee on State Blood Bank

Purpose: To expand the duties of the Committee on State Blood Bank to include organ transplants.

AMENDMENT

Article XI. Divisional Boards and Committees

Section 3. Divisional Standing Committees

Paragraph (F) Scientific Activities Division

(Change name of Committee to read:)

Committee on Organ and Tissue Transfers

Section 5. Duties of Standing Committees

Paragraph 20. (Add following sentence)

The Committee shall also keep abreast of developments in the field of organ and tissue transfers and the procurement, processing and preservation of organs and tissues used in such transfers and shall cooperate with other interested agencies in the establishment and maintaining of high professional standards in the subject areas.

CHANGES OF ADDRESS

Notice of change of address should be sent not less than four weeks prior to the date the change becomes effective. Please send the address label from one of the issues you've just received, which shows code numbers to help us make the change promptly, along with the new address and your zip code.

CONNECTICUT MEDICINE

160 St. Ronan Street

New Haven, Connecticut, 06511

**SUMMARY OF ACTIONS
COUNCIL MEETING**

Wednesday, September 10, 1969

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Granoff, Weber, Jr., Edson, Brandon, Abbot, Gardner, Fabro, Polivy, Rogol, Harwood, Petrie, Wilson, Jr., Purnell, Grant, Nemoin, Friedberg, Johnson, Gorin, Pelz, Root, Jr., Palomba, and Klare.

Also present were: Mrs. Lindquist, Mr. Donelan (AMA), Dr. Patterson (UConn. Med.), Dr. Burnham (Committee on National Legislation), Dr. Foote (State Commissioner of Health), Mr. Villano and Dr. Richards.

Absent were: Drs. Dean, Cramer, Farrell, Roch, McDonald and vonGlahn.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of August 14, 1969.

Life Membership

It was VOTED to approve applications for Life Membership received from the following eligible Active Members:

- Eugene C. Beck, Norwalk (FCMA)—1969
- Elizabeth R. Harrison, New Haven (NHCMA)—1969
- Joseph A. Menousek, Plainville (HCMA)—1970

Committee Appointments, etc.

(a) *Committee on State Blood Bank*: It was VOTED to appoint to membership on this Committee Edward E. Morse, Hartford. Dr. Morse is one of two physicians who are now directing the Red Cross Program, replacing Julius C. Early, Hartford, retired.

(b) *Conn. Postgraduate Seminar In Psychiatry and Neurology*: It was VOTED to reappoint Robert S. McKnight, Hartford, for another three-year term as CSMS representative to this Postgraduate Seminar.

House of Delegates, Date and Place of Semi-Annual Meeting

It being the New Haven County Medical Association's "turn" to host the 1969 semi-annual meeting of the House of Delegates, it was VOTED to accept, with thanks, the invitation for same extended by Kurt Pelz, NHCMA President. Subsequently, the date was set for Thursday, December 11, 1969, and arrangements were made to hold the meeting at the New Haven Medical Association's building in New Haven.

1971 CSMS Annual Meeting, Date and Place of Date of Next Meeting

After considering the possibility of holding the 1971 Annual Meeting (House of Delegates and Scientific Assembly) at a new site (even one out-of-state), the Council VOTED to approve the Hartford Hilton Hotel for the 1971 sessions and the meeting dates of April 27-28-29, 1971.

Date of Next Meeting

The date for the next Council meeting was set for Thursday, October 9, 1969.

CSMS State Legislative Program

Having reviewed a commentary (letter) submitted by the HCMA Board of Directors, and a "Report of the Legislative Division", submitted by Isadore H. Friedberg, Chairman, both of which dealt with the effectiveness of the Society's state legislative program—past, present and future, the Council VOTED to refer both of these documents to a special Ad Hoc Committee (to be appointed by the Chairman) for study and report to the Council. It was further VOTED that the Ad Hoc Committee members be asked to offer their own thoughts on this subject, and that a progress report be filed with the Council at the next meeting (October 9, 1969). Chairman Martin appointed the Ad Hoc Committee as follows:

- Kenneth F. Brandon, Hartford, Chairman
- Charles Polivy, Hartford
- James H. Root, Jr., Waterbury
- Eugene H. Corley, Bridgeport
- David A. Grendon, Sharon
- Jerome K. Freedman, New Haven
- Carl W. Johnson, Thompsonville
- Bernard A. Burnham, Waterbury

CRMP

A number of items having to do with the Connecticut Regional Medical Program were held over from the previous meeting (August 14th), and, in addition, several other communications had been received from or about CRMP in the interim. Following a lengthy, comprehensive discussion of these matters, the Council took the following actions:

(a) *Re-Study of the "High Energy Radiation Services Program"*: It was VOTED to approve, in principle, a CRMP proposal to make a complete re-study of this Program, and to cooperate in the proposed project. It was further VOTED to recommend to CRMP that CSMS representatives be invited to participate in the new study as follows.

Wayne P. Whitcomb, New Haven

David A. Grendon, Sharon
Spinks H. Marsh, Hartford
N. William Wawro, Hartford
Max Taffel, New Haven
Julian Mandell, New Britain

(b) *Related Miscellaneous Actions:* In a series of actions, the Council VOTED to:

- (1) Reaffirm support, in principle, for all specific CRMP programs that have been previously approved.
- (2) Accept the CRMP proposal to review the composition of the Advisory Board and Executive Committee, with specific reference to the number of private practitioners thereon, at the end of the current year (October, 1969).
- (3) Reaffirm that, when the composition of CRMP Board and Executive Committee is reviewed, the Council hold to its original position regarding the number (percentage) of private practitioners.
- (4) Express opinion that CSMS representatives on the CRMP Board and Executive Committee keep the Council informed satisfactorily of CRMP activities under most circumstances, but express appreciation to Dr. Henry T. Clark, Jr., if he will continue to stand by to join the Council, by invitation, to bring the Council up to date on programs or proposals which are of special importance or complexity.
- (5) Accept as information resolutions received from the medical staffs of the Griffin Hospital, Derby, and the Manchester Memorial Hospital, Manchester, both of which voiced support for the Council's position as to the representation of private practitioners on the CRMP Advisory Board and Executive Committee. Further, to publicize to the membership CRMP's agreement to review the composition of those bodies at the end of the current year (October, 1969), and to ask Dr. Clark to furnish the CSMS office with copies of all such resolutions received by CRMP to date.
- (6) Express hope that if Dr. Stanley W. Olson, Director, Division of Regional Medical Programs, visits Connecticut as a guest of CRMP, arrangements might be made, if practical, to have Dr. Olson also meet with the Council or representatives thereof.

COMPAC

It was VOTED to receive as information a report submitted by the COMPAC Ad Hoc Committee to Develop a Plan of Reorganization for COMPAC, and to refer the report, for study and evaluation, to the CSMS Ad Hoc Committee to Study CSMS-COMPAC Relationships, such study and evaluation to include consultation with legal counsel as indicated.

Communication re Employment of Staff Personnel

It was VOTED to refer to the Ad Hoc Committee on Administrative Organization and Planning, for study and report to the Council, a communication received from Charles Polivy, Hartford, in which Dr. Polivy suggested that consideration be given to employing certain additional personnel (an attorney, an actuary, etc.) on a full-time basis to assist in planning and implementing the Society's programs and policies with a view to making same more effective and less burdensome to the elected officers and committee members. The committee was requested to make progress reports at successive meetings of the Council on this and related matters.

Confirmation, Nomination to CMEB

Stevens J. Martin, President, informed the Council that Louis P. Hastings, Hartford, had resigned to Governor Dempsey his current five-year appointment as a member of the Connecticut Medical Examining Board, and that, in conformance with the General Statutes, he proposed to recommend the appointment of Elliot Sicklick, Hartford, as a replacement for Dr. Hastings. The Council gave confirmation to Dr. Sicklick's nomination for this post without dissenting vote. Dr. Hastings is a pathologist; Dr. Sicklick is Associate Pathologist at the St. Francis Hospital, Hartford.

Nominations to Commission on Medicolegal Investigations

An act of the 1969 General Assembly (P.A. 699) created an Office of Medicolegal Investigations, which will operate under the supervision of the above-named Commission. At the suggestion of Commissioner Franklin M. Foote, State Health Department, the Council VOTED to nominate to Governor Dempsey (for appointment of *one* Commission member) a panel of three qualified physicians as follows:

Brae Rafferty, Chaplin
Samuel B. Rentsch, Derby
Donald R. Hazen, Hartford

Memorializing Resolution: John R. Egan

Notice of the death of John R. Egan, Old Saybrook, was received with sadness by the members

of the Council and many expressions of the high esteem in which he was held were voiced. Following the observance of a period of silent prayer, the following memorializing resolution was adopted:

WHEREAS: John R. Egan, M.D., faithfully served the Town of Old Saybrook as a family practitioner, an active church member and an exemplary citizen for more than two decades, and contributed greatly to the health and progress of the community; and

WHEREAS: He served well the Connecticut State Medical Society and his fellow physicians as a member of the Council from the Middlesex County Medical Association for six years, during which he gave generously of his sage counsel and contributed to its deliberations by offering sound judgment tempered with wit and considerateness; and

WHEREAS: All who associated with him on the Council felt privileged to have him as a colleague and to call him friend; and

WHEREAS: To be remembered is never to die; therefore be it

RESOLVED: That the members of the Council of the Connecticut State Medical Society express deep sorrow at the passing of John R. Egan, M.D., and commit to fond remembrance this good friend and valued colleague; and be it further

RESOLVED: That this resolution be spread upon the minutes of the September 10, 1969 meeting of the Council, and that a copy thereof be transmitted to his family.

Resolution: Connecticut Blue Cross' Problems

Having been apprised of the financial problems reported to be facing Connecticut Blue Cross, and believing it to be of the utmost importance to the people of Connecticut that the financial solvency of Blue Cross be preserved, the Council adopted the following resolution:

WHEREAS: Recent testimony by officials of Connecticut Blue Cross before the State Insurance Commissioner indicates that Blue Cross faces a serious financial crisis; and

WHEREAS: This financial crisis has resulted from increases in the costs of hospital services to the degree that Connecticut Blue Cross is currently paying out in hospital service benefits approximately \$1.40 for each \$1.00 collected in subscriber charges (premiums); and

WHEREAS: It is stated by officials of Connecticut Blue Cross that this financial crisis can only be averted by an increase in subscriber charges (premiums) to Blue Cross members; and

WHEREAS: It is of vital importance to the people of Connecticut that Connecticut Blue Cross continue in operation and be financially solvent; therefore be it

RESOLVED: That the Council of the Connecticut State Medical Society express deep concern about the reported financial crisis facing Connecticut Blue Cross and urge the State Insurance Commissioner to take whatever steps are necessary to preserve the financial solvency of Connecticut Blue Cross, such steps to include, if called for, an investigation of the reimbursement agreements between Connecticut Blue Cross and its participating member hospitals.

Reports of Judicial Committee

It was VOTED to accept a multi-item report submitted by the Judicial Committee, and the several sections were then acted upon as follows:

(1) *Disciplinary Proceedings of the Connecticut Medical Examining Board and Public Health Council:* It was VOTED to approve policy recommendations of the Judicial Committee as follows:

- a. That the Connecticut Medical Examining Board be informed of the desire of the CSMS Council and of the Judicial Committee to cooperate fully with the Medical Examining Board.
- b. That the CSMS Council request that the Public Health Council notify the Council of the State Medical Society and the involved county association of all cases adjudicated as soon as possible. (Doctor Edson informed the committee that information was usually restricted during the thirty day period which a physician has for appeal.)
- c. That the CSMS Council request that Doctor Foote notify, if possible, the CSMS Council and county association of all such complaints so that where appropriate, the county can attempt a resolution of the problem.

(2) *Transfer of Original Patient Records:* It was VOTED to approve the subject opinion of the Judicial Committee as follows:

OPINION:

- a. The physical records belong to the physician (M.D.)

- b. It is unethical to transfer or sell the records of the patient to another physician without the patient's request and permission, preferably in writing.
- c. A physician should, when requested by a patient, send the pertinent information to another physician. He need not send the record nor a copy of it.
- d. He, or his estate, should retain the records after he discontinues practice so that information is available to another physician of the patient's choice; and to protect himself in case of a lawsuit, the time dependent on the statute of limitations in his state.

(3) *Publishing of CMEB Disciplinary Actions in CSMS Publications:* It was VOTED to approve the subject policy recommended by the Judicial Committee as follows: That such disciplinary actions can be published in *Connecticut Medicine* when so requested by the Connecticut Medical Examining Board; however, that such publication be limited to the name of the physician involved and the disciplinary action taken by the Board, without further detail.

Acknowledgment of Service by State Senator

It was VOTED to acknowledge, with thanks, the

cooperation and assistance of State Senator Jay W. Jackson, West Hartford, in gaining passage by the 1969 General Assembly of bills establishing a "Uniform Anatomical Gift" statute and instituting the Medical Examiner System in Connecticut.

Communication re Medicaid Payment Policies

Via a communication received from Stewart J. Petrie, Derby, the Council was apprised that claims for payment for services rendered to Medicaid beneficiaries are being returned to physicians with the statement that such claims will not be paid unless the physician's listed charge for the service conforms with the amount allowed by the fee schedule presently in effect. The Council expressed its agreement with Dr. Petrie's contention that since only X number of dollars would be paid anyway (as per the schedule) it is entirely improper for the Welfare Department to insist that the physician, in effect, make it appear as a matter of record that what he is to be paid represents what he normally charges. It is suspected that the Welfare Department is using up its supply of "usual and customary charge" claim forms, and that clerks are under the impression that the amount listed in the fee schedule should appear in the space formerly used to list the physician's "usual" charge. After considerable discussion, it was VOTED to refer Dr. Petrie's communication to the Committee on Third Party Payments for study and report, with the request that the Committee develop a policy statement on the subject matter which would be applicable to all third party payors; i.e., the question of the propriety of any third party payor refusing payment of a physician's claim on the grounds that the fee charged is not in conformance with the payment allowed by a fee schedule.

Survey of Malpractice Coverage and Cost

It being a matter of nationwide concern to physicians that the premiums charged for adequate professional liability (malpractice) insurance coverage are continuing to "skyrocket", year after year, the Council VOTED to request the Committee on Medical Economics and Insurance to undertake a survey of the premiums being charged, and the coverage offered, by all carriers making malpractice insurance available in Connecticut, including the rates for group partnership coverage.

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on August 14, 1969. Detailed minutes of the meeting are on file at 160 St. Ronan St., New Haven, for perusal by any interested member of the Society.*

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Commercial Insurance Company

Electrocardiogram of the Month

Yale-New Haven Hospital
New Haven, Connecticut

Prepared by

HYMAN M. CHERNOFF, M.D.

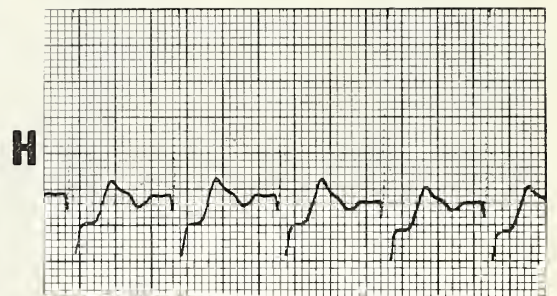
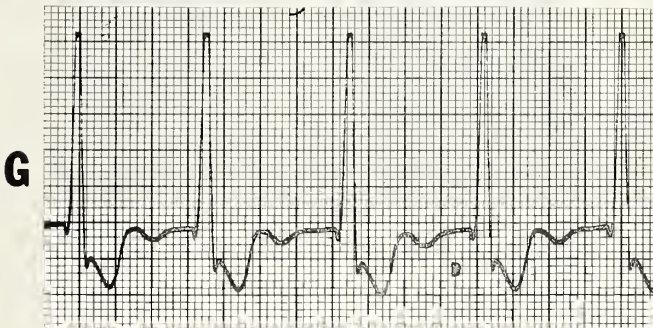
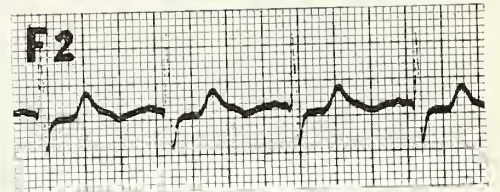
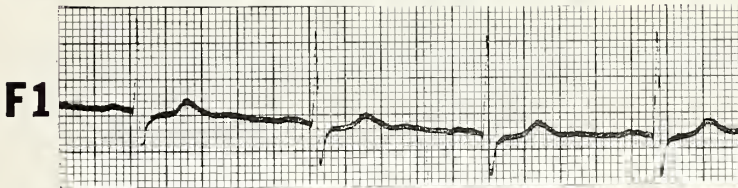
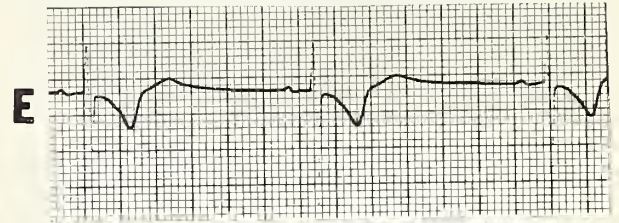
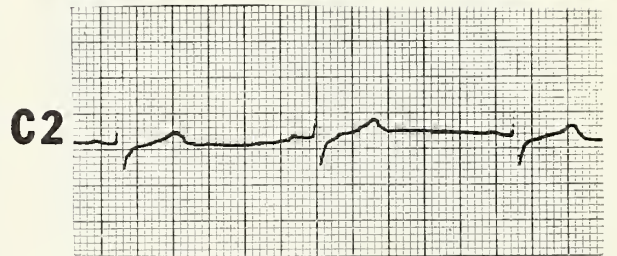
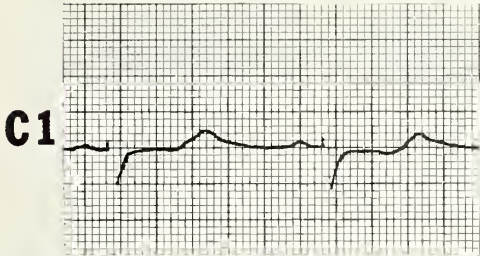
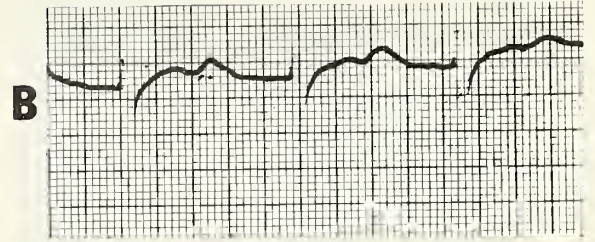
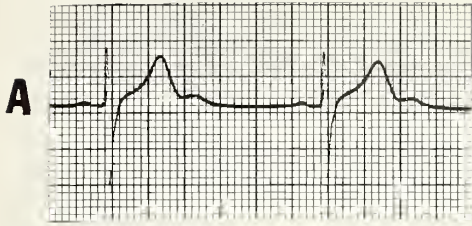
Associate Professor of Clinical Medicine,
Yale School of Medicine

Director, Dept. of Electrocardiography
Memorial Unit, Yale-New Haven Hospital

Although the exact source of the potentials which are responsible for the formation of the U-wave in the electrocardiogram is not definitely known, careful study of this wave is indicated in every tracing since the size, duration, and polarity of the U-wave may be an important clue to the presence of altered electrolyte levels, digitalis and quinidine excess, cardiac pathology, particularly left ventricular hypertrophy or coronary artery disease.

Below are a number of examples of normal and abnormal U-waves and the clinical setting in which they occurred.

- A. This is lead V3 taken in a male, age 20, with no evidence of any cardiac disease or electrolyte disturbance. The positive deflection following the tall T-wave is a normal U-wave. The U-wave may be quite prominent in normal hearts with slow sinus rates.
- B. The large and prolonged positive deflection following the low T-wave in lead V2 is an abnormal U-wave occurring in a patient with coronary artery disease who was receiving large doses of Quinidine to suppress ventricular ectopic activity. Such U-waves should alert one to the possibility of quinidine excess. The quinidine level in this patient was 14 mgm/L.
- C-1. There are large abnormal U-waves in a patient with quinidine level of 18 mgm/L. C-2. Disappearance of the abnormal U-waves 3 days after withdrawal of Quinidine.
- D. Large U-waves are present in lead V5. These follow depressed ST segments. Ventricular ectopic beats are seen to arise from the apex of some of the U-waves. The large U-waves were due to the presence of a low serum potassium level of 2.8. In the presence of low potassium levels ectopic beats are frequently seen to arise during the U-wave period. As first proposed by Nahum and Hoff in 1939, the U-wave corresponds to the supernormal period of ventricular excitability and subthreshold stimuli may more easily depolarize the ventricles during this period. Correction of the low potassium level in this patient led to subsidence of the ventricular ectopic beats.
- E. In this lead V2 there are inverted T-waves, short QT interval and prominent upright U-waves. The patient was receiving digitalis and the serum potassium level was low (3.4). Correction of the potassium level led to subsidence of the prominent U-waves.
- F-1. This is lead V4 in a control tracing taken in a patient with a history consistent with angina prior to performing the Master 2-step exercise tolerance test. The ST segments and U-waves are within normal limits. F-2 is the same lead taken 3 minutes after the exercise. There is segmental depression of the ST segment and inversion of the U-waves. This combination of findings is considered as positive evidence of coronary insufficiency.
- G. This lead V6 was obtained in a 70 year old male with long-standing atrial fibrillation and congestive failure secondary to hypertensive and arteriosclerotic heart disease. Patterns consistent with left ventricular hypertrophy and ischemia are present. The U-waves are deeply inverted. Such inversion of the U-waves is usually associated with severe disease of the left ventricle.
- H. This is lead V5 in a 68 year old female with congestive failure secondary to arteriosclerotic and hypertensive heart disease. The U-waves are inverted. They precede the tiny sinus P-waves. When the sinus P waves are obscure, inverted U-waves may be mistaken for inverted P-waves and a diagnosis of AV junctional rhythm made.



Chest X-Ray of the Month

Section of Chest Diseases

Arnold B. Rilance, M.D.

History

R. P., 45 year old negro male, admitted 5/23/69. For 2 to 3 weeks he had noticed a cough with yellowish-brown sputum. He had smoked 2-3 packages of cigarettes daily for many years. He was an excessive imbibor of alcohol. There was no occupational exposure. Night sweats had been present for several weeks and he had lost 10 pounds of weight. Some sharp pain had been noticed in the left upper chest.

Physical Examination:

Diminished breath sounds, left upper chest posteriorly. Clubbing of fingers and toes was noted.

Laboratory Studies:

Sputum—negative for AFB x 3
Sputum Cytology—negative x 3
Bronchoscopy—negative

Scalene Node Biopsy—negative

Metastatic Series—negative

Liver Scan—normal

Bronchial brushing—negative for malignant cells

Tuberculin Test—positive

An exploratory thoracotomy and left upper lobectomy was performed on 6/24/69.

Pathological report: Atelectasis with organized interstitial pneumonia. Bronchiolitis obliterans, Chronic lung abscess.

Discussion

The onset of illness is indefinite. On admission the most likely diagnosis was considered to be primary bronchogenic carcinoma.

At thoracotomy a chronic lung abscess with organized pneumonia was demonstrated.



Figure 1

Chest X-ray on admission. Dense atelectatic infiltration apical segment, left upper lobe.



Figure 2

Following bronchodilator and drainage therapy, abscess cavities demonstrated.

DR. ARNOLD B. RILANCE, Director, Winchester Chest Clinics, Yale-New Haven Medical Center.



Figure 3

Following four weeks of medical regimen. IPPB drainage, antibiotics. Note decreased size of cavity.



Figure 4

Laminogram (8 cm.) demonstrating large, shaggy, thick-walled abscess ? cavity.

Members of the Connecticut State Medical Society reading papers before other organizations are requested to submit their papers to the JOURNAL for consideration by the Board of Editors for publication. Please send them to:

LOUIS H. NAHUM, M.D., *Editor*
CONNECTICUT MEDICINE
160 St. Ronan Street
New Haven, Connecticut 06511

OBITUARIES

Robert F. Jones, M.D.

1919-1969

Dr. Robert F. Jones of Old Lyme died suddenly on August 29, 1969, of a coronary occlusion. He was in the private practice of psychiatry for the past three years in New London.



Dr. Jones grew up in Middletown where he attended public schools. He was graduated from Wesleyan University. He then entered the United States Army Air Force and served four years as a bombardier. He was shot down twice in combat and was a prisoner of war for one year. After the war, he attended the College of Physicians and Surgeons at Columbia University and then interned at the Hartford Hospital. He took his psychiatric training at the Institute of Pennsylvania Hospital. He then entered the United States Air Force in which he served with distinction until his retirement as Lieutenant Colonel in 1966. In his last tour of duty as Chief of Psychiatry at the United States Air Force Academy, he developed a great interest in the psychiatric problems of young adults, an interest he continued in his private practice. He returned to his beloved southeastern Connecticut following his retirement.

Dr. Jones was a member of the American Medical Association, the American Psychiatrists Association and the Connecticut State Medical Society.

He is survived by four daughters, Mrs. John W. McBride and the Misses Patricia, Christie and Tracy Jones.

Frank G. Marx, M.D.

John R. Egan, M.D.

1916-1969

Dr. John R. Egan, a well respected and hard working general practitioner of Old Saybrook, died in the Yale New Haven Hospital on September 6, 1969 after a long illness.

Dr. Egan, born in Nebraska on August 19, 1916, graduated from Harvard University in 1938 and received his M.D. degree in 1942 from Duke University. He interned on the Second Medical Service at Boston City Hospital and received further training at John Hopkins Hospital in Baltimore and St. Mary's Hospital in Pierre, South Dakota.

After serving in the United States Army Medical Corps from 1944 to 1947, Dr. Egan entered general practice in Washington, D.C. In 1949 he moved to Old Saybrook where he soon had a very busy general practice in which he gave unstintingly of himself and his time until ill health forced him to slow down, a hard thing for Jack to do.

During this time Dr. Egan was an active member of the Connecticut State Medical Society and the Middlesex County Medical Association. He was an elected delegate of Middlesex County to the Connecticut State Medical Society House of Delegates from 1954-1960, and elected alternate councilor and then councilor from 1960-1968. He was also a member of the American Medical Association. This period of most conscientious service covered 14 years from 1954 to 1968.

Dr. Egan was active in his church, Grace Episcopal Church, Old Saybrook, serving as Vestryman and vice-warden from 1960 to 1966.

He is survived by his mother; his wife, Mrs. Marjorie Sampson Egan; three sons, two daughters and one grandchild.

All Jack's many patients, friends and colleagues join in his family's grieving for our great loss.

A. W. Thomson, Jr., M.D.

In Memoriam

Nolan, John F., Stratford, McGill University 1932. Dr. Nolan was a surgeon for many years in the Fairfield area. He was a former chief of staff at the Bridgeport Hospital. Dr. Nolan was a past president of the Bridgeport Medical Society, a member

of the board of trustees of the Fairfield County Medical Association and a member of the Council of the Connecticut State Medical Society. Dr. Nolan was a member of the American Medical Association, Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Nolan died September 14 at the age of 64.

Ting, Me I., University of Michigan 1920. Dr. Ting was a general practitioner at the Connecticut State Farm for Women before she moved to Massachusetts in 1964. Dr. Ting was a member of the American Medical Association, New London County Medical Association and the Connecticut State Medical Society. Dr. Ting died July 15 at the age of 69.

Placement Opportunities

PHYSICIAN, to cover every other weekend and certain holidays, a well organized general practice consisting mostly of adults, and no one under the age of ten. Salary is \$1300.00 a year plus the fees collected.

HOUSE PHYSICIAN, full time, to cover emergency room and house. Night coverage. Must have Connecticut license. Apartment provided; good fringe benefits. Write P.O. Box 3494, Bridgeport, Connecticut 06605.

GENERAL PRACTITIONER, for additional Senior Physician at the Connecticut State Prison. Opportunity exists for part time outside practice if desired, in nice community. Salary range \$16,370.00 to \$19,970.00. Three weeks vacation, plus sick leave, eleven paid holidays, three annual earned leave days, time off for medical meetings. Excellent health insurance. Contact Mr. Parson, Personnel Department, Connecticut State Prison, Somers, Connecticut 06071.

ONE YEAR PSYCHIATRIC RESIDENCY at 3rd year level for year beginning July, 1970. AMA approved. Unique opportunity to prepare for private practice and community psychiatry. Supervised intensive, dynamically oriented psychotherapy emphasized. Experience in meaningful application of psychopharmacological agent and somatotherapy. Work with adults and children in residential and outpatient setting. Stipend \$16,500 per annum, with major medical insurance benefits. For information, write Charles P. Neumann, M.D., Medical Director,

The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

CHIEF OF MEDICINE—At accredited State Veterans general medical and surgical hospital of 496 beds, with a domiciliary section of 800 beds. Hartford area. Duties: Directs the facility's program in medicine; related work as required. Age limit: Up to 65 years, if in good health. Experience and training: Completion of general internship in AMA-approved hospital, and not less than 5 years employment with emphasis in the field of medicine and/or certain equivalent qualifications to be evaluated individually. Salary range—Open. For further information and application forms, write to: Frank Mongillo, M.D., Chairman, Veterans Home and Hospital Commission, Rocky Hill, Connecticut.

GENERALISTS, INTERNISTS AND PEDIATRICIANS—Northern Connecticut city of 47,000 in need of 2 General Practitioners, 2 Internists and 1 Pediatrician. Can readily be assimilated into physician community over next 3 years. Hospital privileges available; also good office space available near hospital. Those interested in establishing solo practice in the fields named may obtain further information from: Martin Duke, M.D., Director of Medical Education, Manchester Memorial Hospital, Manchester, Connecticut 06040.

DERMATOLOGIST WANTED — Board certified or eligible, Army requirements fulfilled, for association with New Haven Dermatologist with active and growing practice.

PEDIATRICIAN — Two newly associated, young pediatricians already desire third man to associate in busy and very interesting general pediatric practice. No investment necessary. Equal time off. Salary to early partnership.

INTERNISTS — Northwestern Connecticut Hospital area needs internists interested in practicing general internal medicine. Hospital area serves a 50,000 population.

Great opportunity for Internists, General Practitioners, Otolaryngologist, Psychiatrists and Pediatricians in the Windham area. Solo or group practice available with hospital staff privileges. For further information contact: Frank Bird, M.D., Windham Community Memorial Hospital, Mansfield Avenue, Willimantic 06226.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

WOMAN'S AUXILIARY

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Mrs. James F. Jones, Danielson

President-Elect

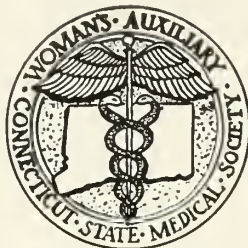
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Christmas Is A Time For Sharing

Get into the Christmas spirit this year by supporting medical education and research through the purchase of personalized Christmas cards . . . selected especially for AMA-ERF. Proceeds from the sale of these cards are credited to your woman's auxiliary AMA-ERF committee and help support the Foundation. Your order assures the success of a future medical education or a promising research project.

About AMA-ERF

The Woman's Auxiliary project for the American Medical Association Education and Research Foundation consists of two branches: (1) Funds for Medical Schools, and (2) the Institute for Biomedical Research, both of which are supported by AMA-ERF. Through project such as greeting card sales and your fund-raising activities, medical education and research will be able to continue and expand.

Funds For Medical Schools

Experts now estimate that by 1975, we will need at least 400,000 physicians—100,000 *more* than we now have in the U.S. In order to reach this goal, we must be able to equip our medical schools to prepare the intelligent and dedicated young people who are willing to spend years and money for a medical career.

The cost of providing quality medical education is tremendous and growing rapidly each year. Often, educating more physicians means acquiring larger and better facilities, additional equipment, and more faculty members. Your AMA-ERF funds provide this kind of flexible financial aid, and medical school deans receive this money without strings attached to use as they see fit to cope with their most pressing financial problems.

Proceeds From The Sale Of AMA-ERF Cards Help Support The Work Of The Institute For Biomedical Research

The Institute for Biomedical Research is dedicated to the principle of pure research. It allows talented scientists to carry on exhaustive studies in their chosen fields without the restrictions of teaching assignments or administrative duties.

For Tomorrow's Health Team . . .

An unusual multi-lingual "Job Fair for Health Careers" held at the Waterbury, Conn., YWCA was aimed at showing people who don't speak English well that there can be a future for them in the health field. The New Haven County medical auxiliary and the "Third Wednesday at the YW" committee sponsored the fair.

The programs and door signs were printed in three languages—Spanish, Italian and English. Interpreters were present to translate presentations which included talks by Garland L. Weidner, MD, Waterbury public health director, and Miss Eleanor McGuire, RN, assistant education director, Connecticut Regional Medical Programs. The film, "Horizons Unlimited," also was shown, and sections on jobs ranging from nursing and medical technology to kitchen, laundry and maintenance work were conducted by personnel from Waterbury and St. Mary's hospitals. Six women and two girls signed up on the spot to take a practical nursing course.

Many of the 150 attendees (who ranged from high school age up to 65) were attracted through "New Opportunities for Waterbury," a program to open up jobs to minorities. Announcements were also sent to Puerto Rican, Italian and Portuguese clubs as well as to schools and churches.

"The director of the 'New Opportunities' program has not stopped raving about the fair," said Mrs. Mehdi Eslami, 1968-69 New Haven County

auxiliary president. "He said that this was the first program in our city which presented careers so that the ethnic groups he works with could understand them."

A plus was the interest and involvement of the YW's "Third Wednesday" committee, largely made up of persons 65 and over. They handled registration, passed out pamphlets and directed the participants to the sections they were interested in.

"The cooperation we received was overwhelming," said Mrs. Eslami. "I knocked at every door and received help. I used all the information I had gathered from MD's Wife and the *Direct Line* newsletter and gathered material on almost 200 fields of medical service.

MEETINGS

GENERAL

November 4, 5, 6

26th Annual New England Postgraduate Assembly
Statler Hilton Hotel, Boston

Sponsored by the Council of New England State Medical Societies

Program acceptable for 21 prescribed hours by A.A.G.P.

Registration fee: \$25.00

December 11 2:00 P.M.
Semi-Annual Meeting, Connecticut State Medical Society House of Delegates

New Haven County Medical Association Building
364 Whitney Avenue, New Haven

May 12, 13, 14

178th Annual Meeting
Connecticut State Medical Society House of Delegates
Hartford-Hilton Hotel, Hartford

MEDICINE

Weekly Oncology Courses 12 Noon
Hospital of St. Raphael, Radiation Therapy Conference Room

November 20, Case Presentation; December 4, Alkylating Agents, David S. Fischer, M.D.; December 11, Case Presentation; December 18, Antimetabolites, Joseph R. Bertino, M.D.

December 12 8:30 A.M.-5:30 P.M.
Peter Bent Brigham Postgraduate Medical Series
Boston, Mass.

"Common Thyroid Disorders, Diagnosis and Management"

Herbert Selenkow, M.D., Director, Thyroid Laboratory

PEDIATRICS

November 19

Annual Pediatric Symposium

St. Francis Hospital, Hartford

"Principles of Immunology and Infectious Diseases Applied to the Care of Children"

Speakers: John B. Robbins, M.D., Marshall Horwitz, M.D., Mark Abramowicz, M.D., Jules Titelbaum, M.D., Debora Wolfson, M.D., all of the faculty of the Albert Einstein College of Medicine

Contact William E. Hart, M.D., Director of Pediatrics, St. Francis Hospital

SURGERY

January 15, 1970

Conference, Connecticut Chapter of the American College of Surgeons

Park Plaza Hotel, New Haven

Contact Francis M. Hall, M.D., 140 Woodland Street, Hartford

Doctor's Office

Stewart Atkinson, M.D., announces his association with William P. Keefe, M.D. and Joseph C. Carpentieri, M.D. for the practice of ophthalmology at 240 Ashley Street, Hartford.

Michael Hersen, M.D., announces the opening of an office for the practice of psychology at 8 West Street, Danbury.

Richard F. Jones, III, M.D., announces his association with G. Lawrence Austin, Jr., M.D. in the practice of obstetrics and gynecology with offices at 85 Jefferson Street, Hartford and 711 Cottage Grove Road, Bloomfield.

Robert A. Lanzi, M.D., announces the opening of an office for the practice of allergy at 380 Boston Post Road, Orange.

Howard Shapiro, M.D., announces his association with Daniel Adler, M.D. and James Rutherford, M.D. for the practice of obstetrics and gynecology at 131 Kings Highway North, Westport.

Harold C. Walker, M.D., announces the removal of his office to 10 Mott Avenue, Norwalk.

Gordon B. Wheeler, M.D., announces the opening of an office for the practice of medicine at West Main Street, Chester.

AROUND THE STATE

New Haven County

Board of Governors

New Haven County Medical Association

The Board of Governors of the New Haven County Medical Association met on September 25, 1969 at the Colonial House in Hamden.

The Connecticut State Medical Society accepted the invitation of our President, Dr. Kurt Pelz, to hold the semi-annual meeting for 1969 in New Haven County. The Connecticut State Medical Society semi-annual meeting will take place at 2:00 p.m. at the New Haven Medical Association Building, 362 Whitney Avenue, and a social hour will follow.

Dr. Allen Traurig of Waterbury was elected to the committee on Credentials and Orientation. Dr. Mehdi Eslami was nominated for membership in the Conn. State Medical Society Allied Medical Services Committee for the Connecticut Regional Medical Program.

The Public Relations Committee is planning a county-wide survey of attitudes and opinions of area physicians. Doctors Root and Granoff reported that studies on the new role of COMPAC as it relates to the state and county societies is well under way.

Our Councilor, Dr. Stewart J. Petrie reported on recent actions by the Connecticut State Medical Society Council. The financial problems of Blue Cross; changes in the approach of our State Legislative Committee for the current bienium; support of the specific CRMP programs already approved, and the re-affirmation of the need for broader physician participation on the CRMP executive committee; and current difficulties with the present Medicaid program were all elaborated upon by Dr. Petrie.

The Review Committee, under the chairmanship of Dr. Kurt Pelz, has continued to place a heavy burden on the time of all its members. Appreciation was expressed to the members of the New Haven County Medical Association's Review Committee for their dedicated service on this very active and crucial committee.

A considerable amount of discussion took place on how best to implement the one-man, one-vote principle regarding the apportionment of delegates to the various local areas of the county. A mathematical formula to fairly apportion areas was established.

New Haven County, for the first time in Connecticut, began a county-wide program of photograph-

ing all its members on September 19, 1969. The program is in co-operation with the Connecticut State Medical Society plan to have photographs of all Connecticut physicians available.

The possibility of a New Haven County Medical Association sponsored group vacation flight and tour to various parts of world in the spring of 1970 is currently being investigated.

A social hour and dinner followed the meeting.

Respectfully submitted,

William L. West, M.D., Clerk

Placement Wanted

ORTHOPEDICS—37 years of age, Board certified with National Boards desires partnership in Connecticut. Military obligation completed. Available immediately.

G.P.—desires emergency room position, experienced, age 50, presently in own practice.

SURGEON—38 years of age Board certified interested in a group type practice. Presently in practice. Available immediately.

INTERNIST—32 years of age, Board certified with National Boards, desires full time hospital position in cardiology, will consider partnership. Presently in practice.

OPHTHALMOLOGIST—30 years of age, Board certified with National Boards, interested in an associate type practice.

PATHOLOGIST—32 years of age, Board eligible desires associate practice in Connecticut. Presently in practice, available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Hyperbaric Oxygen In Hemorrhagic Shock

(R. S. Amonic et al—*JAMA*, 208: 2051, June 16, 1969) A Jehovah's Witness patient bled massively from rectum but refused blood transfusion. At eventual operation a bleeding gastric leiomyoma was excised. His hemoglobin value fell to 2.2 gm./100 ml. and on the third postoperative day he showed evidence of severe cerebral and myocardial ischemia and congestive heart failure developed. Hyperbaric oxygen therapy caused a reversal of all signs and symptoms of hypoxia and the patient recovered. At 1 atmosphere pressure blood has 0.3 volume per cent of oxygen dissolved in plasma. At 2 atmosphere with a subject breathing 100 per cent oxygen, the blood plasma contains 4 volume per cent sufficient to sustain life in a patient with greatly diminished hemoglobin value.—L.H.N.

XYY Chromosome: Premature Conclusions

(Seymour Kessler and Rudolph H. Moos: *Science*, 165: 442, August 1, 1969) No strong correlation exists between the presence of an extra Y chromosome and any behavioral, morphological or physiological parameter except perhaps a tendency to increased height.

It is a pure myth that XYY males are uncontrollably aggressive psychopaths. In institutions XYY males seem in fact to be less violent and aggressive and their preadmission histories generally involve crimes against poverty rather than persons. Furthermore, several XYY individuals without behavioral dysfunction or criminal tendencies have already been identified.

The research on XYY individuals to date has not ruled out familial, social and other non-genetic factors as the major determinants of the characteristics attributed to the extra Y chromosome. Also there is no evidence whatsoever to indicate that XY and XYY males tend to differentially benefit from different rehabilitation procedures.

The authors point out that the legal and medical implications of findings in this area increase the usual responsibility of the investigator to be circumspect and cautious in drawing conclusions on the present evidence. They urge prospective studies of

XYY individuals detected at birth, to help clarify some of the relevant factors that contribute to behavioral deviances in some XYY individuals.—L.H.N.

Cause Of Tay-Sachs Disease Is Uncovered

(*JAMA*, 209: 1298, September 1, 1969) The cause of infantile amaurotic familial idiocy (Tay-Sachs disease) has been shown by Dr. John S. O'Brien to be caused by absence of an enzyme hexo-aminidase A. This enzyme is supposed to prevent the ganglioside from accumulating in neural tissue and destroying it. If the enzyme is absent in amniotic fluid, it will open the possibility of in-utero screening early enough to give parents the opportunity of a therapeutic abortion.

Tay-Sachs disease can sometimes be diagnosed at birth from a "cherry-red" spot in the eye of the newborn. Children with the disease appear otherwise normal until between the sixth and twelfth month when they become irritable, begin to react excessively to noises and sometimes "forget" how to sit. Eventually the child becomes deaf, blind and paralyzed.

The enzyme molecule must be present in the brain. Giving it to such children will be of no help because the molecule is too big to pass the blood brain barrier.

"The best hope we have is for prevention the same as with other conditions caused by a recessive gene" said Dr. O'Brien. Some day Dr. O'Brien thinks we'll probably have cards listing the diseases we carry on our chromosomes and people will compare cards before having children.—L.H.N.

Influenza: Recommendations For Immunization

(U.S. Public Health Service Advisory Committee on Immunization Practices: *Ann. Intern. Med.*, 71: 617, September 1969.) Both standard and highly purified bivalent vaccines will be available.

It is not recommended for healthy adults and children. Vaccines should be considered only for persons of any age with chronic debilitating conditions, older persons who may have incipient or potential chronic disease, particularly cardiovascular and bronchopulmonary diseases.

Persons at high risk who regularly receive influenza vaccines and had one or more doses of Hong Kong strain last year require only a single full dose booster of bivalent vaccine.

Immunization should be scheduled for completion by early December.

Local or mild systemic reactions to standard influenza vaccines are common. They occur up to 50 per cent of adults and appear to be related primarily to the non-viral components of the vaccine.

Individuals who should receive influenza vaccine but have had severe local or systemic reactions to the standard vaccine might be given a highly purified vaccine subcutaneously.

Influenza vaccine should not be administered to anyone who is hypersensitive to eggs because the vaccine viruses are grown in embryonated chicken eggs.—L.H.N.

Magnesium And Digitalis Toxicity

(Seller, R. H. and Moyer, J. A.: *The Heart Bulletin*, 18: 32, 1969) Potassium protects the heart against digitalis toxicity and potassium depletion sensitizes the myocardium to development of digitalis toxicity. In general excess magnesium produces electrocardiographic changes characteristic of excess potassium and vice versa.

Many diuretic drugs cause not only hypokalemia but also hypomagnesemia and both those electrolyte deficiencies may pre dispose to the development of digitalis toxicity. Hypomagnesemia has been reported in patients with malabsorption syndrome, chronic alcoholism, prolonged or severe loss of body fluids, hyperparathyroidism, primary aldosteronism, hepatic cirrhosis and diabetic acidosis.

It seems advisable to evaluate the serum level of magnesium as well as potassium when arrhythmias caused by toxicity follow the administration of cardiac glycosides. For patients who are found to be hypomagnesemic the slow (1 cc. min.) intravenous infusion of 10 to 20 cc. of 20 per cent magnesium sulphate given during electrocardiographic monitoring may have significant therapeutic value.—L.H.N.

Preoperative Digitalization For Non-Cardiac Cases Harmful?

(*JAMA*, 208: 458, April 21, 1969) Some thoracic surgeons digitalize their non-cardiac patients. Dr. George L. Juler believes that prophylactic digitalization of non-cardiac cases does decrease over-all mortality from post-operative congestive failure. However, preoperative digitalization increased over-all mortality by post-operative cardiac arrhythmias of a wide variety such as atrial fibrillation and flutter, cardiac arrest, premature ventricular systoles and paroxysmal atrial tachycardia.

Heart surgeons digitalize prophylactically with undoubted benefit but non-cardiac digitalization especially in older patients apparently should not be carried out. Apparently there occurred a five-fold increase in the incidence of post-operative arrhythmias in patients who had been digitalized in the absence of clinically apparent cardiac disease. Digitalis causes loss of potassium from myocardial cells and this renders them more subject to arrhythmias.—L.H.N.

Carotid Flow May Predict Strokes

(*JAMA*, 208: 780, May 5, 1969) Dr. Glenn W. Kindt of the University of Michigan has used an ultrasound technique which causes no discomfort to the patient to record carotid artery blood flow. The patient lies motionless without any premedication. A mask is placed over the face and a transducer over the common carotid artery. The patient is then given a mixture of inspired air containing 5 per cent or 7 per cent CO₂ for approximately three minutes.

The portable instruments then measure flow through the skin by recording the difference in the frequency of the sound emitted compared to that reflected. This frequency difference is proportional to the blood flow velocity. Twenty normal subjects increased their carotid flow on an average of 48 per cent with inhalation of CO₂ whereas five persons with cerebrovascular occlusive disease had little or no response. This permits the identification of the asymptomatic person who is likely to have an ischemic cerebrovascular accident.

Surgical approach might be reconstructive of the occluded vessel. Medical measures such as control of hypertension, diabetes, obesity and smoking are also likely to be of greater benefit when applied prophylactically and early.—L.H.N.

NEW BOOKS IN REVIEW

THE PERSON: HIS DEVELOPMENT THROUGHOUT THE LIFE CYCLE. Edited by Theodore Lidz. Basic Books, Publishers, 404 Park Avenue South, New York, NEW YORK, 10016, 1968. 608 pp. \$10.00.

Reviewed by: LOUIS H. NAHUM

This is a great book. It has many things for many people. Its appeal will be much wider than the medical student for whom it is written. Psychologists, social workers, counselors from various disciplines, lawyers and even pastoral counselors can no longer afford to pursue their labors without familiarity with the contents of this book.

The Person is the story of the unfolding of the individual human life from birth to death. It views the person in the total context of his life, as a member of society and a family and as endowed by his biological and cultural inheritance. He deals with infancy, the toddler, childhood integration, the juvenile, adolescence, occupational choice, marital choice and marital adjustment, parenthood, the middle years and old age. Professor Lidz draws upon the resources of all disciplines: critical periods in behavioral development, the stages in childhood development as described by Piaget, the insights of dynamic psychiatry and psychoanalysis. The findings of biological and behavioral sciences are unified to describe the inherited and psychosocial forces that mold personality from the beginning to the end of life. In short it is a classic textbook on personality development.

The book carries a strong message that as we learn dynamics of the development of the person we shall learn how best to strive to produce the best kind of person and in the process how best to understand each person. This is especially important for the physician. And so the author states that his purpose in writing this book has been to provide medical students with a guide for learning about the persons who will be their patients. At the same time many other professionals and laymen also require a similar comprehensive understanding of people. It will also have value to persons who are simply interested in the "proper study of mankind."

The confluence of psychoanalytic and psychobiologic approach in this book reflects the authors own psychiatric training. He became a psychoanalyst after reading Freud. His clinical and investigative interest in psychosomatic disorders and in schizophrenia have required major theoretic reconceptualizations of theories which were based primarily on studies of neurotic patients. This led him to a study of the nature of man and human adaptation, especially man's unique capacities, his ways of coping with his environment and surviving its hazards. Man's neuromuscular system has made him capable of using tools particularly that "tool of tools—language." The nature of the consequences of the development of language is set out in the first two chapters, the human endowment and the family and then developed throughout the book.

To incorporate language and thought into the description and conceptualization of the person's development, the author utilized Piaget studies and others also. The prolonged helplessness and dependency, the late puberty, the dependence upon language and upon learning adaptive techniques, the

need to provide prolonged care for offspring and many other such factors tend to lead to common features in all people and also set a sequential pattern of the phases of the life cycle.

The author's opening remarks to medical students are eloquent in their humanity and wisdom and beautifully expressed in almost aphoristic form. The student he tells them is not simply a spectator but "an active participant in the drama of peoples lives." "One cannot come to know very much about others without learning to know oneself," how one's life fits together and how one defends against insecurities and anxieties. "Everyone has defects, weaknesses, hidden shames and guilts, but they are usually offset if not balanced by assets." "There is ample room in society for difference and divergence and few persons are capable of understanding others who have not been made alert to their own shortcomings and insecurities." "Tolerance of others may well start with tolerance of self."

The physician's sensitivity to suffering and a constant awareness of what illness means to a patient and his family cannot but cause him pain. He has need for defenses against too great an involvement. Such defenses are proper and necessary and valuable . . . but can become deleterious. He must not withdraw from learning what is meaningful in the lives of patients. Becoming indifferent is not the most useful way to withstand the stresses. With trained understanding of people and their ways of reacting the physician can serve as a guide to the patient who is confronted by unfamiliar experiences, new stresses and is lost among his concerns and involvement. The adage know thyself is intimately related to "the proper study of mankind is man." "To care for the patient means to care for the patient." As one can see the style of the book is almost aphoristic frequently epigrammatic reflecting the great knowledge, wisdom and humanity of the author.

The final chapter on life patterns describes the basic themes encountered in people. They are more readily detected in emotionally disturbed persons because they are more set, more clearly repetitive, although repetitive ways of reacting and relating occur in all our lives. To understand the meaning of an episode in a life can often be grasped properly only through understanding how it furthers, impedes or disrupts essential themes. This chapter is extremely informative and can be read as a thing in itself, but must be more than read. It must be grasped, digested and capable of being reproduced by the reader. It is an education in itself.

With each incoming class there is a run on the book at the booksellers. There is reason for its great popularity.

ABDOMINAL PAIN, A GUIDE TO RAPID DIAGNOSIS. Edited by Lars-Erik Gelin, M.D., Lloyd M. Nyhus, M.D. and Robert E. Condon, M.D. J. B. Lippincott Company, Philadelphia, Pa. 123 pages, 26 figures, 7 tables. Published May 28, 1969, \$8.00.

Reviewed by: IRA S. GOLDENBERG

Abdominal pain is not a symptom restricted only to surgical patients, but can and does occur quite often in non-surgical circumstances. Unfortunately, however, a patient with ab-

dominal pain usually is categorized as an operative candidate and is referred, often without an in-person evaluation by his physician, to a surgeon for diagnosis and treatment. This is probably a good thing for some patients whose pain indicates a probable intraperitoneal problem for which an operation will be necessary. But many patients with abdominal pain do not have the need for a surgeon's services and often waste a great deal of time and effort during an unnecessary surgical consultation. How idyllic it would be if all physicians—internists, pediatricians, surgeons—recognized the significance of a particular patient's abdominal complaints as a manifestation of any one of a varied number of pathological states. This book could contribute materially to such an enlightened era if it will be read and digested by all physicians.

Here in succinct description and apt illustration is presented the essence of abdominal pain as the "first symptom" and the authors leave nothing to the imagination of the reader regarding diagnosis. Special attention is given to types of pain and the significance of their locations, "the patient's complaints and what they mean", and detailed discussions follow devoted to clinical examination, differential diagnosis, abdominal trauma, extraperitoneal disease involving abdominal pain, pediatric abdominal pain and an entire chapter about acute appendicitis, the commonest cause for abdominal pain demanding surgical care.

At first glance this book of compact size and clear typography would seem to belong on the shelf of the medical student or the surgical house officer. It does belong there, certainly, because it is one of the best of many books written on this topic. It belongs even more logically, however, in the library of all physicians who ever evaluate abdominal pain and want to improve their care of the sick.

ATLAS OF NUCLEAR MEDICINE—VOLUME I. BRAIN.
By Frank H. DeLand, M.D., and Henry N. Wagner, Jr., M.D. W. B. Saunders Company, Philadelphia, 1969. 217 pp. 383 illustrations. \$18.00.

Reviewed by: RICHARD P. SPENCER

Brain scans are based upon the fact that certain substances injected intravenously will distribute themselves into most body spaces, but not into the brain (being excluded by what has been referred to as a blood-brain-barrier). When intracranial pathology is present, the injected material tends to enter the lesion. If the injected substance is radioactive (emitting a gamma ray), its distribution can be mapped out by appropriate scanning devices. The rapid growth of brain scanning attests to its usefulness as a relatively innocuous procedure with a high diagnostic yield. Working on the assumption that an appreciation of the distribution pattern of the radiopharmaceutical might permit a more specific diagnosis, DeLand and Wagner have produced an atlas of brain scans. These scans, from the Nuclear Medicine Department at Johns Hopkins, are presented with information as to the clinical problem, the diagnostic impression prior to the scan, a description of the scan, its interpretation, and the final anatomic diagnosis.

After a brief introduction that includes mention of the criteria for evaluating a scan, the normal anatomy of the brain (as visualized on the scan) is discussed. This is followed by sections on variants in the scans, congenital anomalies, infectious diseases, trauma, cerebrovascular diseases, and tumors. The two following sections, on diseases of the skull

and scalp, point out an area that may confuse the interpretation of brain scans. The final section of the book is devoted to cisternography (radioisotopic studies on cerebrospinal fluid circulation).

The atlas is presented in logical fashion, with the scans correlated with the pertinent radiographs. The quality of the reproductions is good, although there is no mention of the problems encountered in obtaining the same scan image time after time (Figures 26a and 26d for example likely show how small differences in technique can bring the transverse sinus into or out of focus). There are few defects in the book, although the micro-sign has infrequently misplaced the milli-designation (as on Page 194). The scans are of the relatively static situation, some minutes after injection of the radio-nuclide. Perhaps future editions will include frames from the dynamic studies in which the injected bolus is followed through the cerebral vasculature. Volume I of the atlas is a welcome edition to the literature of Nuclear Medicine. We look forward to the other volumes of the series.

PHYSIOLOGY OF THE GASTROINTESTINAL TRACT.
Edited by E. Clinton Texter, Jr., M.D., Ching-Chung Chou, M.D., Higinio C. Laureta, M.D. and Gaston R. Vautrappen, M.D. The C. V. Mosby Co., St Louis, 1968. 262 pp. with 106 illustrations. \$10.75.

Reviewed by: LOUIS H. NAHUM

The modern physician needs a sound working knowledge of anatomy, biochemistry, physiology and pharmacology if he is to deal with the ever expanding technical aspects of medicine and at the same time maintain a critically informed attitude toward the flood of new information available after leaving medical school.

This is one of a series of volumes in physiology in which the authors have tried, and most successfully, to delineate the areas of physiologic knowledge most relevant to medical practice. In the first part the regional circulation is dealt with. This is followed by pertinent reading references.

It is a very worthwhile book for students of medicine and gastroenterologists who will be referring to it often for physiologic reference.

MEDICAL INTERVIEWING: A PROGRAMMED MANUAL. *Edited by Robert E. Froelich, M.D. and F. Marian Bishop, Ph.D., M.S.P.H. The C. V. Mosby Company, Saint Louis, 1969. 116 pp. \$4.75.*

Reviewed by: STEPHEN FLECK

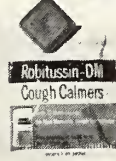
This small paperback volume of some hundred pages is a kind of old-fashioned cookbook on interviewing but not of French cuisine calibre. It is not "programmed" because presenting a series of interview vignettes followed by multiple choice questions as to right or wrong is not programming in the pedagogical sense. The approach to interviewing is extremely simple and mostly in question-and-answer form. The focus is directed more to the student or reader than to the patient although adequate attention is being paid to non-verbal elements of communication in the book. However the data organization is lacking in any psychological or social sophistication. In particular no effort is made to help the student understand family dynamics, although presumably this is geared at the medical student who intends to become a general practitioner or family physician. The book is not recommended.



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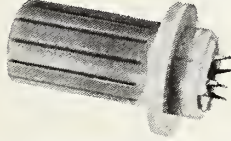
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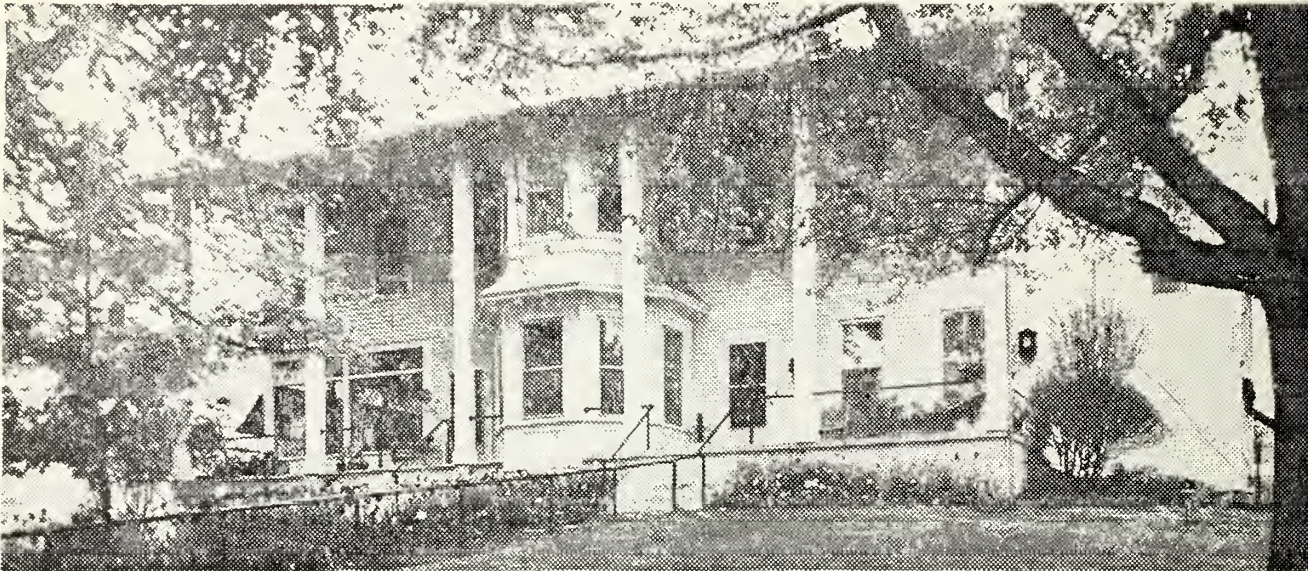


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Reflections On The Cyclamate Ban

On October 18, 1969 the FDA suddenly banned cyclamate. The decision was based on the finding of bladder cancer in 8 of an initial 80 rats who received the highest levels of cyclamate, 2,500 mg/kg/day, together with one per cent saccharin. In two other groups of 80 animals, each of which received 500 mg/kg and 1,000 mg/kg, no tumors were found. The rats received this sweetener throughout their adult lives in doses which were enough to sate the sweet tooth of a horse. They then developed an "unusual" form of cancer. No effort was made to determine whether the results were due to cyclamate, saccharin a synergistic action between the two or some unknown factor. At such doses it might even be surprising that only one out of 10 rats developed tumors.

Throughout the years that cyclamate has been consumed by an estimated 150 million humans, no evidence has appeared linking cyclamate to human cancer. In fact, on October 8, 1969, Abbott scientists at a seminar emphasized that cyclamates were considered completely safe. Until now, the FDA recommended daily intake not to exceed 3.5 grams per day. The amount which "caused" cancer in one out of ten rats over a lifetime was 50 times the recommended daily dosage limit in humans, equivalent to drinking 350 bottles of diet cola per day.

An independent pharmacologist has described these results as "crushingly disappointing"^{2, 3} words which the committee themselves must have surely mouthed as they wondered how to arrive at a balanced verdict. A British wag² has insisted that the guilty verdict on cyclamate was arrived at in applying McPherson's rule, an ancient tenet of Scottish law which holds that when two men have been drinking, one of them a known drunkard, and the other man starts a fight it is always the drunkard that gets the blame. Applying this rule, the committee must have found that since saccharin has been used for a "longer" time than cyclamate without "apparently" harmful effects, it must have been the cyclamate which caused the tumors. After such reasoning it must have been easy to hold it prudent to stop further addition of cyclamate to food. One would have supposed that cyclamate pre-

sented some kind of hazard to human health. The substance could not have been banned more quickly if the new evidence had shown that cyclamate is transmuted to arsenic in the body!

The hazards of interpreting toxicological work are well known. In the case of cyclamate for example it has been shown that subcutaneous injections of cyclohexylamine, a derivative, produce cancer in rats, but so far that matter do injections of salt. Then there are reports that cyclamates induce breakages in the chromosomes of white blood cells, an ominous finding to be sure but meaningless because no one knows what harm, if any, damaged leucocyte chromosomes do. Despite the obvious reasons for caution, the health authorities of Finland, Sweden, and then Britain followed the FDA in banning cyclamate. Unless these organizations were better informed than their counterparts in this country, they possessed no further evidence against cyclamate than did the FDA which based its action upon results that should have been more carefully confirmed and their implications understood.

There are some preliminary experiments which demonstrated that cyclamate and cholesterol pellets implanted into mouse bladder caused tumor as did cyclamate when injected into the bladder. Malformations have been reported in 15 per cent of chick embryos injected with cyclamate, and as noted above cyclamate has been implicated in chromosomal breaks. According to the mass media the decision was made to ban cyclamate after a HEW official called a "hurried meeting of a scientific panel". We must remember that many products both food and drugs are on the market which have been proven to be carcinogenic, teratogenic or mutagenic, that are still available to the public. It would seem that the action on cyclamate was premature, of too great import to be made by a few government officials at a "hurried meeting" without thorough investigation and review by the scientific community.

Before the results of scientific experiments can be accepted as conclusive several criteria must first be satisfied. One is that the experiments should be reproducible in the laboratory of the original authors and by independent investigators. Then

the agent in question should be tested in other animal species and other biologic systems to determine whether the results are species specific or have broader biologic significance. To test the specificity of the agent, controls should be injected or implanted with other materials in a parallel manner to the agent being investigated. Furthermore the results must be analyzed in statistical terms which generally mean large scale experimentation. If positive results are obtained, basic research should be conducted into the mechanism of action of the substance. Finally epidemiologic data should be collected in prospective and retrospective studies to determine whether any undesirable effects have been produced. Epidemiologic information is especially pertinent to the cyclamate question since millions of Americans including pregnant women have consumed vast quantities of this compound.

The production of bladder cancer was the recent discovery that led to this precipitous decision. It is claimed that FDA acted on the Delaney amendment of 1958 which holds that any substance "known" to cause cancer in humans or animals must be kept off the market. What then do we know about bladder cancer. For over 50 years cancer of the bladder has been recognized as an occupational disease in persons working in coal tar aniline dye industry.³ While many measures are taken to protect the health of these workers and of the consumers of their products none-the-less this industry has not been eliminated. Crayons and hair coloring are readily available. Tryptophan an amino acid found in proteins has been shown to be carcinogenic for the urinary bladder.⁴ Must we now all become vegetarians? Both laboratory and epidemiologic studies conclusively demonstrate that cigarette smoking causes many diseases one of which is bladder cancer. Yet in the 20 year period during which cyclamate has been so widely used there has been no increase in the mortality from bladder cancer.⁵ Neither have cigarettes been taken off the market.

Regarding teratogenicity and chromosome damage resulting from cyclamate, contrary to the results in chick embryos, studies in other animals such as rats were negative.⁶ Furthermore a variety of foods and drugs have been found to be teratogenic in one or more species. Excess vitamin D in the rabbit, hypervitaminosis A in the rat,⁷ cortisone in some strains of mice,⁸ and aspirin in the rat,⁹ are prime examples. Chromosome breakage in vivo has been produced by cyclohexylamine, a metabolite produced in the intestinal tract by a small percentage

of animals. However, with the usual rate of conversion, a huge amount of cyclamate would be required to show this effect.¹⁰ Work in Inhorn's laboratory^{6, 9} has shown no mutagenic effect when very high concentrations of cyclamate were put into cultures of normal human cells.

There remains to be considered the other half of the equation. What will be the consequences of restricting the availability of sweeteners? First of all we know that millions of diabetics who have finally been able to obtain a palatable and varied diet, will certainly suffer and perhaps increase sucrose intake. Persons who are prediabetic or have a genetic predisposition to diabetes may without artificial sweeteners increase sucrose intake and develop full blown diabetes. Sucrose has now been correlated with development of coronary heart disease and absence of artificial sweeteners could promote advancing atherosclerosis. The dental profession has acclaimed the role of cyclamates in the prevention of tooth decay. Children now happily take baby aspirin and penicillin because they have been sweetened. Certainly a major nutritional problem in America today is obesity. Individuals who are attempting to limit their caloric intake will be handicapped by the cyclamate ban.

Can we afford to lose the positive benefits of this chemical? According to the news releases a new sweetener will be available by January 1, 1970. How can this product be adequately tested in such a short period of time, compared to the 10 year developmental period of careful testing of cyclamate prior to 1950? How can the FDA guarantee that the new product will not eventually be found to produce carcinoma of the left adrenal in Chinese hamsters?

When there is so much human data available, it is inconceivable that cyclamate be discarded on the basis of experiments in which one out of ten rats who received enormous doses of cyclamate, plus saccharin over an adult lifetime developed an unusual form of bladder cancer.

L.H.N.

References

1. HEW Soured on Artificial Sweetener JAMA 210 795 Nov. 3, 1969.
- 1a. Inhorn, S. L., Cyclamate Ban. Science. 166. 685, Nov. 7, 1969.
2. The Cyclamate Bandwagon. Nature, 224. 298, Oct. 25, 1969.
- 2a. How McPherson's Rule sank Cyclamates. Nature, 224. 398, Nov. 1, 1966.

3. Ackerman, L. V., and Del Regato, J. A. *Cancer—Diagnosis, Treatment and Prognosis*. Mosby. St. Louis, Mo. Ed. 1, 1962. p. 821.
4. Allen, M. J., Bayland, E., Dukes, C. E., Horing, E. S., Watson, J. G. *Brit. J. Cancer*. 11. 212, 1957. Cancer of the Urinary bladder induced in mice with metabolites of Aromatic Amines and Tryptophan.
5. Eisenberg, H., Odoardo, D. F., Campbell, T. C. *Cancer in Connecticut Mortality Data 1949-1961*. Conn. State Dept. of Health, Hartford 1964. p. 68; 1969. *Cancer Facts and Figures*. American Cancer Society, New York 1969.
6. Stoltz, D. R., Khera, K., Bendall, R., Gunner, S. Cytogenetic studies with cyclamate metabolites" talk given at the Eighth Somatic Cell Genetics Conference Oct. 7, 1969 at Chatham, Mass.
7. Barrow, M. V. in *Birth Defects Original Article Series 5*. D. Bergsma. Ed. National Foundation, New York, 1969. pp. 202-206.
8. Wilson, J. G., Warkany, J. *Teratology Principles and Techniques* (Univ. of Chicago Press, Chicago 1965). p. 35.
9. Goldman, A. S., Yakovac, W. C. *Arch. Environ. Health*, 8, 648, 1964. Salicylate Intoxication and Congenital Anomalies.
10. Legator, M. S., Palmer, K. A., Green, S., Peterson, K. *W. Science*. 165. 1139, 1969. Cytogenetic studies in rats of Cyclohexylamine. A metabolite of Cyclamate.

Alcoholic Heart Disease

Electrocardiographic signs indicating existence of alcoholic cardiomyopathies were shown to consist of either picket fence T or wing shaped T or non-specific alterations.¹ There is also evidence besides the alterations in the electrocardiogram which supports the view that alcohol exerts a depressant effect on cardiac contractility. Wendt and his associates² have recently demonstrated in chronic alcoholics, an enzymatic abnormality especially of malic dehydrogenase. This means that intramitochondrial enzymes are affected by clinical alcoholism even in patients without clinical evidence of heart disease. Further support comes from the work of Gimeno and his associates³ who studied the effects of alcohol in the isolated rat atrium. They found an almost linear relation to exist between the concentration of alcohol and the decline in myocardial contractility.

Recently Regan et al⁴ studied a group of alcoholic patients who seemed to have normal cardiovascular findings but mild to moderate increase amounts of fat in liver but without cirrhosis. They found that such patients response to exercise was not normal, however, but rather resembled the findings in patients who had known cardiac disease. These observations certainly show that the alcoholic patient without clinical evidence of cardiac disease can nevertheless exhibit an abnormal ventricular response to exercise.

Gould and his associates⁵ has previously studied ten alcoholic patients who exhibited impaired cardiac response to exercise, and also had a presystolic gallop. They asked themselves two important questions. The first was whether patients with alcoholic heart disease always also have liver disease. The second question raised was whether all alcoholic patients had left ventricular dysfunction. To obtain answers to these questions they have now reported their findings on fifteen hospitalized males ages 35-57 with a long history of alcoholic intake. In this series none had hepatic insufficiency. All had normal sized livers and none had symptoms referable to the cardiovascular system.

The procedures used for the investigation consisted of retrograde arterial catheterization through a brachial arteriotomy. Then they catheterized the pulmonary artery. They were then able to obtain left ventricular, pulmonary arterial, systemic arterial pressure and cardiac output at rest and after a given degree of exercise by pedaling a bicycle ergometer for 6-7 minutes while in the supine position. The left ventricular end-diastolic volume was calculated cineangiographically. Shortly after the exercise cardiac catheterization and liver biopsies were performed on 12 of the 15 patients. They discerned 2 groups: 6 had a high resting cardiac output. Of these 3 had presystolic gallop and 3 also had fatty livers. Of a second group of 9, 3 had presystolic gallops and 4 had fatty livers.

The findings revealed that a high resting cardiac output can occur in alcoholics without liver disease and it is the alcohol not the liver disease that causes cardiac dysfunction. It is also clear that a high resting cardiac output can occur with or without a presystolic gallop. This means that when we hear a presystolic gallop in an alcoholic patient even without obvious cardiac disease, the sign represents cardiac dysfunction and we must conclude he has a decrease in left ventricular contractility.

It would appear reasonable to assume that the excessive intake of alcohol does produce an impairment in the metabolic and contractile properties of the left ventricle and the resulting decline in hemodynamic function may not be readily discerned in a patient in the resting state. Furthermore, such hemodynamic abnormalities can occur in a well-nourished alcoholic patient who has not had an alcoholic beverage for months.

Alcoholism is widespread in this and many other countries. We must now recognize that alcoholic heart disease is a very common abnormality. It can remain months after alcohol has been discontinued.

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What we need to know is the ultimate fate of such patients. This knowledge should be of great theoretical and practical interest.

L.H.N.

References

1. Nahum, L. H.: Alcoholic cardiomyopathy. *Conn. Med.*, 25: 493, August 1961.
2. Wendt, V. E. et al: Hemodynamic and metabolic effects of chronic alcoholism in man. *Am. J. Cardiol.*, 15: 175, 1965.
3. Gimeno, H. L., Gimeno, M.F. and Webb, J. L.: Effect of ethanol on cellular membrane potential and contractility of isolated rat atrium. *Am. J. Physiol.*, 203: 194, 1962.
4. Regan, T. J. et al: The myocardial effects of acute and chronic usage of ethanol in man. *Trans. Ass. Amer. Physicians*, 78: 282, 1965.
5. Gould, L., Mohammad, Z., Mahmood, S. and DiLieto, M.: Cardiac hemodynamics in alcoholic heart disease. *Ann. Intern. Med.*, 71: 543, 1969.

The Computer In Medicine

The modern electronic computer was first built in World War II. They have gone a long way since then for now they are no longer calculating machines. They have become an information processing instrument which is reshaping many aspects of our lives.

A computer is strictly speaking a calculating machine. It is primarily an electronic machine capable of manipulating numbers or symbols after they have been translated into electrical impulses. The digital computer deals with discrete units that are represented in the computer by separate electrical impulses and can be compared with the channel selector of a TV set. Analog computers deal with continuously changing variables that are represented in the computer by currents or voltages and thus can be compared with the volume control or brightness control in the TV set. Analog computers are used primarily in medicine for physiologic studies such as the analysis of cardiovascular, pulmonary or neurophysiologic data. For processing, however, analog signals are first converted into digital form.

The modern electronic computer consists of 5 elements, input devices, output devices, arithmetic units, control units and memory storage units. Each of these parts varies in a variety of ways and has become quite diversified. For example the input units can be punch cards, magnetic tapes and magnetic discs, magnetic readers and even transducers. A new approach still in the developmental stage is the use of video terminals usually coupled with a light pen. Direct entry of data may be accomplished

by using keyboard instruments, especially convenient for persons skilled in typing.

The output devices are the reverse of input and translate the electrical impulse from the computer into a more meaningful form. This output may be printing produced on a typewriter or live printer or it may be in the form of a drawing or diagram or punched card or punched paper tape, magnetic tape or disc or even a cathode ray display. The convenience of the input terminals and appropriateness and usefulness of the output terminals will determine whether physicians can use this remarkable information processing technology beneficially in the practice of medicine.

The element in the computer that stores the data and instructions is called "the central processing unit" and consists of memory storage and logic circuitry. The computer is basically designed to add electrical impulses, subtract, multiply and divide and perform certain logical operations on the basis of this ability. There is a control unit which coordinates the movement of the data from memory to the arithmetic unit and back as needed for processing. The unit also interprets the user's instruction which are also called "the program."

The computer will not lead to new insights. The user must first have clearly in mind what he wants done with his data but how he wants the product presented to him. He needs to prepare a detailed step-by-step set of instructions (program) for the computer in a code language that it understands. This process is called programming.

Most information can be collected over some convenient period, stored then analyzed or processed in batches at a time convenient for the computer operator. The computer has turned out to be the best teacher to a physician or investigator as to how to develop clarity of thoughts. For example if an investigator wants to make use of a computer to find out how certain blood chemistry values vary with clinical manifestations of a certain disease, he must define clearly the problem and the form and control of the answers he expects. He must decide what clinical manifestations he wishes to study, whether to separate his cases into primary and secondary forms. He must then separate the secondary forms into those resulting from medication and those resulting from or associated with other diseases. He must be certain that data collection is uniform and he must understand computer facilities available for processing the data and the form in which the output is to be presented. Only after these steps is he ready to begin preparing the program.

There is a tendency to equate the use of computers in medicine with diagnosis by computer. Actually diagnosis is the one aspect of information handling in medicine most difficult to describe in terms of simple logic and therefore one of the most difficult to accomplish by computer. For the diagnostic process involves not only the collection and weighing of signs and symptoms but also the intellectual skill of pattern recognition. As Mayne states it "humans use the latter to zero in on a solution whereas computers must count out among all the possibilities." Until we understand our diagnostic processes better and until we can define more specifically the data we use for making medical decisions the use of the computer in the diagnostic process must remain difficult.

There are other uses of the computer in medicine which at present seem more feasible. Business aspects of hospitals could profit. Ordering, scheduling and reporting laboratory tests or medical consultations could profit. So could physiologic monitoring of electrocardiograms in intensive care units. A patient's temperature, blood pressure, pulse rate as well can be sensed and recorded frequently. Current practices in the automated interpretation of laboratory tests such as the computer analyses of electrocardiograms and radioisotope scans. Computers could be used in the medical library to store and retrieve information that will require indexing the medical literature and interpreting its content. The problems in achieving this are enormous but the advantages would be great. Medical records could be transmitted with extreme rapidity from one area to another for use in patient care and would be much better organized and more legible than many contemporary written records.

One of the primary difficulties to be faced in utilizing computer technology in medicine remains how to define the data physicians use in making medical decisions and discovery, how a physician uses these data for his decisions. Such information is required for the many steps involved in designing a computer based system and in writing the program. It is probable that computers will be most effective in medicine when physicians are able to find new methods for providing health care services that will unite at once the speed and memory of these remarkable information processing machines with the judgment and "pattern recognition" abilities of the physician. When this comes about one great physician will become the teacher of all.

In any event let us not forget that a computer is not a doctor. It does not have in the person of a

physician the human qualities of respect, concern, sympathy and understanding which no machine can ever duplicate.

L.H.N.

Reference

1. Mayne, J. G.: The computer and its potential for medicine. *Ann. Int. Med.*, 70: 207, January 1969.

The Thymus And Host Resistance

The time is now at hand when the thymus must be added to the accepted list of endocrine glands. It produces several humoral agents which play a fundamental role in the regulation of the structure and function of lymphoid tissue. As a consequence of this regulatory influence on lymphoid tissue in addition to other effects attributed to the thymus and lymphatic system, it plays an important role in host immunological competence. Earlier White and his associates had proposed the hypothesis that lymphoid structures participate in humoral mechanisms concerned with immune globulin synthesis.¹ They demonstrated that normal lymphocytes contain gammaglobulin and these lymphocytes and also malignant proliferating lymphocytes from immunized animals contain and have the capacity to synthesize antibodies. Thus came our understanding of the functional significance of the lymphocyte in antibody production and in immune phenomena.

The next step was the demonstration that a protein fraction from calf thymus tissue produced an increase in the weight of lymphoid tissue in the rat and an absolute increase in the number of blood lymphocytes. It was then a simple step to demonstrate that this substance also occurs in other animals and was termed lymphocyte stimulating factor (L.S.F.).

On the other hand if the thymus is removed neonatally it leads to a deficiency of the lymphoid population of the blood and lymphoid tissue. Such an animal loses the ability to exhibit most cell-mediated responses. It develops a syndrome described as a "wasting disease": It fails to grow normally, exhibits atrophic symptoms and dies within several months. Such animals show inability to make antibodies to some antigens. These effects of early thymectomy are a general phenomenon since they occur in a variety of experimental animals including birds.

Thymectomy in older animals may also lead to a slow diminution of the lymphocyte population and alteration of those phenomena dependent on the normal number and function of these cells. The

whole syndrome of thymic ablation can be prevented if the animal receives thymic tissue or thymic transplants are carried out. This will prevent "wasting disease" and restore immunological responsiveness in neonatally thymectomized animals.

Now White et al have described their experiments on the effect of calf thymus extracts. One of these they termed Thymosin, which they purified and then found evidence that it produces gross increases of lymph node weight. This was confirmed biochemically by increased incorporation of precursors of DNA-RNA and protein into lymph nodes. It was also confirmed histologically by sharp increases in mitotic activity of lymphocytes. Thymosin lymphopoietic activity has also been demonstrated to occur in thymic tissue of a variety of animals, rabbit, rat, guinea pigs, hogs and humans. It is significant also that per gram of thymus, thymosin content of older animals is as great or even greater than in the young. Clearly the thymus remains active throughout life.

White and his colleagues report investigations on two aspects of the role of the thymus in host immunological competence: its influence on cell-mediated immune processes (CMI) as reflected in the homograft response and also humoral antibody production as revealed by the capacity to synthesize antibody. Their experiments which were models of scientific reasoning and were meticulously performed did indeed show that thymosin can function in lieu of the thymus in thymectomized animals by endowing the host with specific capacity to reject skin allografts. Animals without the thymuses can reject a histo-incompatible skin graft, but their response to an antigenic challenge did not appear to be significantly restored. The conclusion from such work is warranted that thymosin influences cell-mediated immune phenomena and does not have a role in humoral antibody phenomena.

Lymphoid tissue is especially sensitive to ionizing radiation. The question thus presents itself as to whether thymosin can increase the rate of regeneration of lymphoid tissue in animals subjected to whole body x-irradiation. After irradiation there is a significant decrease in lymphoid mass in mice which persists for 72 hours. The irradiated mice when treated with thymosin showed a rapid restoration of lymph node mass which returned to normal after 72 hours. The mitotic activity of such lymphocytes was greatly increased as might be expected in a rapidly regenerating tissue.

Of obvious interest is the question of whether this observed stimulation by thymosin is of functional

significance, that is whether thymosin can be useful in attenuating either prophylactically or remedially the deleterious effects of irradiation on the structure and function of lymphoid tissue. Their preliminary still unpublished data do indeed suggest that the life of adult mice exposed to lethal doses of whole body x-irradiation may be prolonged significantly by daily administration of thymosin provided it is begun immediately post-irradiation.

Some other interesting observations relate to the effect of thymosin on spleen cells in thymectomized mice. The results show that such cells can be made to participate in cellular mediated immune response. On the other hand in contrast to thymosin spleen extracts have no such capacity.

Two questions remain. One is whether there are present in the thymus multiple humoral factors not just thymosin alone. Another is what might be the possible clinical application of thymic preparations. Its use in whole body irradiation is already known. Others are sure to follow when a rational approach to possible clinical application of thymic preparations can be undertaken. It is clear, however, that the thymus is an endocrine gland and that its humoral roles are of prime significance in the regulation of host resistance.

L.H.N.

Reference

1. White, A. and Goldstein, A. L.: The role of the thymus gland in the hormonal regulation of host resistance. Presented at Ciba Symposium, New Delhi, India, 1969.

Recommendations On Use Of Rubella Vaccine

The Council on Environmental and Public Health has just released its recommendations on rubella vaccine which deserves the careful scrutiny by the Profession and forms the basis for a coordinated plan to be developed jointly by state and local public health agencies in cooperation with state and local medical associations.

The primary goal of rubella vaccinations is of course the prevention of the congenital rubella syndrome. Secondary goals are preventing rubella in post-pubertal patients where disabilities are usually more serious than the relatively mild disease that it causes in young children.

There are presently two vaccines available and a third in experimental stage. One is grown on duck embryo cell culture. One is grown on rabbit kidney cell culture and the third with a different virus

strain is being grown on human embryo lung cell culture.

The currently licensed vaccine is administered by a single subcutaneous injection of reconstituted lyophilized vaccine. The following precautions are recommended in insert instructions. Pregnant women must not be given the vaccine because the viremia that follows vaccination and lasts two to six weeks may pass the placental barrier and affect the growing fetus. Safeguards must also be taken if vaccination of a non-pregnant woman in the child bearing age is anticipated. To avoid the possibility of her becoming pregnant, pregnancy should be delayed by several months to ensure that no damage can occur to a beginning fetus.

The Merck, Sharp and Dohme vaccine is grown on duck embryo cells and therefore should not be given to individuals that are sensitive to duck or chicken eggs or feathers. Furthermore, the vaccine contains 25 micrograms of neomycin so that individuals sensitive to this drug should not receive vaccine.

Maternal immune antibodies cross the placental barrier and these interfere with the development of immunity in children under one year of age. Accordingly the vaccine should not be given to children until after they have reached one year of age.

The presence of other virus diseases or any febrile active generalized infection as well as the use of cortico-steroids, irradiation, alkylating agents, or anti-metabolites or other agents that weaken the normal defense mechanisms of the individual contraindicate the use of rubella vaccine. Other contraindications include concurrent use of a different live virus such as measles or poliomyelitis. In such a case rubella vaccine should be deferred for at least four to six weeks.

We must bear in mind that the vaccine currently available is still relatively new (about 13,000 susceptible children had been observed for adverse reactions prior to licensing) it is possible than un-anticipated adverse reactions particularly in older patients may occur with general use. Such adverse reactions should be reported promptly to the State Health Department and to the manufacturer who is responsible for reporting it to the Division of Biologic Standards of the N.I.H.

It is estimated that only 15 per cent of the children under five years of age have become immune through naturally acquired disease. This incidence increases in older age groups. Approximately one-third show natural immunity in ages five to nine,

60 per cent in ten to fourteen year olds, 75 per cent in fifteen to nineteen year olds and 85-90 per cent of those twenty to thirty-nine year olds.

These figures vary from community to community, but may be used as a general guide for the desirability of performing screening tests for susceptibility prior to giving the vaccine.

For widespread use in view of the lack of adverse reactions in small children and the fact that two-thirds of the children under ten would be susceptible all should receive vaccine without doing a preliminary serological test for susceptibility.

Children in kindergarten and the early grades of elementary school deserve initial priority for vaccination because they are commonly a major source of virus dissemination in the community. A history of rubella illness is usually not reliable enough to exclude children from immunization.

It is likely that prior to the next seasonal peak which would be anticipated in spring of 1970, millions of doses of the three different rubella vaccines will be available for use.

L.H.N.

Cardiotoxic Effects Of Phenothiazines And Imipramine

Sudden deaths can occur from overdosage of chronic use of tranquilizers. This is the substance of a report by Richardson et al.¹ With histological and histochemical techniques, they demonstrated acid mucopolysaccharide material in and around the arterio capillary bed particularly in the sub-endocardial region. When we reflect that abnormal electrocardiograms were found in patients taking phenothiazines and also in patients and experimental animals acutely poisoned with imipramine or its analogs as observed by Gaultier et al.² it is reasonable to assume that they are caused by pathological changes similar to those described by Richardson et al in the case of phenothiazines. Like the phenothiazines, disturbed a-v and i-v conduction were commonly encountered as well as T wave changes.³ Furthermore, man seems to be more susceptible than some experimental animals, for the lethal dose is one-tenth that for mice per kg. body weight.

From the literature one gains the impression that electrocardiographic abnormalities and cardiac toxicity are reversible when the drug is stopped. However, Alexander's⁴ experience is not so opti-

mistic. He in fact found that damage to the heart by these drugs can be serious and permanent.

When one reflects on the large numbers of patients in institutions taking the drugs on a chronic basis, and without detailed evaluations of their cardiovascular status, the true prevalence of cardiac toxicity is unknown. There are isolated reports such as those of Leesma and Koenig⁵ in neuropsychiatric journals which presently constitutes the main source of information regarding the possible hazards of these drugs.

The serious side effects which may occur when drugs are taken in short periods are readily observed and publicized. This is not the case in instances of insidious cumulative toxicity accompanying the chronic use of drugs for months or years. Psychotropic drugs the phenothiazines and psycho-energizers such as imipramine and related compounds are in widespread use today and are being administered over long periods of time. They constitute an important part in the management of serious psychoneurotic and psychotic disorders. Without much question they have changed the dismal prognosis of such patients and have greatly reduced long-term incarceration in mental institutions.

The total medical needs of institutional patients can be readily overlooked especially when their improvement is felicitous from the use of drugs. In such a setting it is not surprising that manifestations of drug toxicity have gone unrecognized. The obvious suggestion is, in the light of the known toxicity of phenothiazines and imipramine in a setting where they are chronically administered over long periods, that a cardiological evaluation including a chest X-ray and an electrocardiogram be carried out at the most at six month intervals.

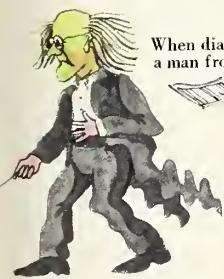
One must search for cardiomegaly and the appearance of abnormal electrocardiographic changes. Once discovered it requires reappraisal of the neuropsychiatric situation and judgment whether it is severe enough to justify the continued use of a possibly life threatening cardiotoxic drug.

We still do not have firm data on acute and chronic toxicity of these drugs in animals after 6-8 months of administration. But we have man himself who now serves as the experimental subject in many institutions throughout the world. How the cruel dilemma will be resolved when the psychiatric condition of a patient requires the drugs and his physical condition precludes their use, will become an important exercise in how to evaluate the alternatives that are presently open.

L.H.N.



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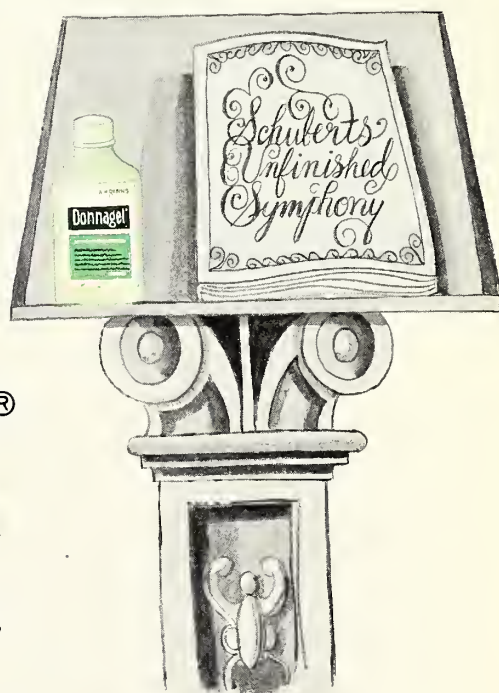




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Nasal, Sinus Decongestant_____				•	
Non-narcotic_____	•	•		•	•

References

1. Richardson, H. L., Graupner, K. E. and Richardson, M. E.: Intra myocardial lesions in patients dying suddenly and unexpectedly. *JAMA*, 195: 254, 1966.
2. Gaultier, M., Boissier, J. R., Gorceix, A. and Simon, P.: Cardiotoxicity of imipramine in man and animals. *Proc. European Soc. Study Drug Toxicity*, 6: 163, 171, 1965.
3. Ban, T. A. and St. Jean, A.: Effect of phenothiazines on the electrocardiogram. *Canad. Med. Assoc. J.*, 91: 537, 1964.
4. Alexander, C. S.: Cardiotoxic effects of phenothiazine and related drugs. *Circulation*, 38: 1014, 1968.
5. Leesma, J. E. and Koenig, K. L.: Sudden death and phenothiazines. *Arch. Gen. Psychiat.*, 18: 137, 1968.

Slowing Down The March Of Time

Professor Aloys Tappel of the University of California at Davis has proposed a theory of aging as being caused by a series of reactions in the body triggered by free radicals that are released when O_2 reacts with certain fatty substances or lipids in the body. There have been many speculations about the causation of senescence in organisms but Tappel's theory is an attempt at accommodating several of them under a single hypothesis. We would all like to believe a hypothesis that would permit us to correct the aging process simply with employing doses of readily available antioxidants such as vitamin E and C, and sulphur containing amino acids and selenium.

Tappel holds that the aging process develops from a sequence of reactions that occur in the following chronological order. First is peroxidation of polyunsaturated lipids resulting in the formation of free-radical intermediate products. Peroxidation involves the direct reaction of O_2 and lipid to form stable peroxidases. The second step is the interaction of free radicals with cell membranes and enzymes resulting in the disruption of their structure and function through polymerization and protein chain-scission reactions. In his third step specific damage occurs to lysosomes which are intracellular bodies that destroy cell compounds. This leads to body tissue destruction and formation of the so-called "age pigments."

Age pigments are complexes of proteins and lipid which characteristically accumulate in the brain, heart and muscle tissue of aged persons. The function of these pigments is unknown, but their composition suggests to Professor Tappel that they originate from peroxidized lipids that were not fully digested by lysosomal enzymes. The peroxidized lipids themselves, Tappel explains, are probably

portions of membranes that were damaged by free radical interaction and then digested by lysosomes. Such damaged membranes could only be partially destroyed and thus they accumulate in the lysosomes where they somehow deteriorate into age pigments.

Tappel analyzed age pigments and found the presence of enzymes typical of both lysosomes and mitochondria. The inference from this is warranted that damaged mitochondrial membranes could be a major contributor to the inside parts of age pigments. The finding of peroxidized lipids in age pigment is the strongest evidence of the role of lipid peroxidation processes and their free radical intermediates in aging. We might suppose, therefore, that such aging processes might presumably be slowed by biological antioxidants and free radical scavengers. Vitamin E and C, methionine and butylated hydroxytoluene are such substances. Accordingly Tappel suggests a daily regime of .5-1.0 gm. vitamin E, 200 mg. vitamin C, 1 gram of methionine and a dose of .02 per cent of body fat of butylated hydroxytoluene (the FDA approved level). Even though the method is strictly experimental none of the substances recommended could be harmful.

There are other ideas on the cause of aging, for example that it is a genetically programmed species specific series of events and another that accumulated somatic mutations finally lead to the breakdown of regenerating mechanisms in cells.¹ Tappel has omitted these possibilities from his scheme, and this might prove self defeating right at the outset. Long before the recent data from biochemical genetics were available, there was much indirect evidence for the existence of genetic control of the life span. For example that longevity is a heritable property. Twins tend to have the same life expectancy. Polyploidism (possession of more than two sets of chromosomes) tend to affect life span and mutagenic agents reduce life expectancy.

The biochemical data for the genetic theory have emerged chiefly for studies that correlate tissue age with gene activity through DNA-RNA hybridization studies. Many such studies have been performed and while the results are ambiguous and are subject to a variety of interpretations, they have been consistent with the theory that there is a differential in gene activity between young and old tissues.

The hybridization experiments have taken two forms. In one type single stranded DNA is extracted from tissue of various ages and is bonded to acetylphosphocellulose polymers of synthetic hybrid. If aging affects the ability of DNA to form synthetic

hybrid then the base sequence segments of DNA that produce aging may be revealed in washings containing deleted bases.

In the second type of experiment DNA-RNA hybrids from tissues of various ages are separated into DNA-RNA strands and the base sequence compared. If the base sequence in DNA of young and old tissues are the same but the base sequences of RNA are different then the pattern of active genes in aging cells may be decipherable from the RNA copy of the active gene.

If Tappel is right, however, then it would be ironic if the oxygen upon which our lives depend were also responsible for that invariably fatal syndrome—aging.

L.H.N.

References

1. Don't breathe: oxygen may be aging you. *Scientific Research*, 4: 25, September 1969.
2. Nahum, L. H.: Protection against natural aging by antioxidants. *Conn. Med.*, 33: 303, May 1969.

Is The World Heading For An Environmental Crisis

Is the world heading for an environmental crisis if pollution continues unchecked? Professor Barry Commoner of Washington University, St. Louis has thought for some time that this will happen. He cited examples of modern technology, nuclear reactors, artificial fertilizers, gasoline engines, and pesticides which have stretched "the will of the ecosystem." But he said also that there is hope of making technology conform to the powerful restraints of the living environment. There is one particularly optimistic sign of public concern in this country about pollution of air, water and soil in the formation in the past year of student environmental groups, the importance of voluntary bodies working together cooperatively. Similar bodies are also being set up in Britain. The question, of course, is whether this will be effective enough.

Thoughts such as those of Professor Commoner are pointing to the need for urgent action so as to avoid the disasters of which modern technology is capable. The problem is important because it raises the question of what society can expect from the development of science in the years ahead. At the same time we must keep in perspective that some science and technology has enormously improved society in the past century or even the past decade. Infant mortality is declining. The expectation of

life is rising. It has brought prosperity to certain areas. The development of tele-communication has been an almost unmitigated blessing.

But what is the value of all this supposed progress if it should be accompanied by catastrophe. This is the question underlying a good deal of the anxiety in the past few years about the social role of technology. Technology has brought us nuclear weapons and it is safe to say that if they were to be used it could put the clock back decades or even centuries. In warfare there are now only Pyrrhic victories and so the strategic concept of deterrence has built up. If society is intelligent there is reason to hope that it can surmount technology's threat to its existence. The potential side effects of other developments in technology such as extensive water pollution, air pollution and land pollution by DDT can be controlled by harnessing technology into the service of man.

Technology is really an instrument of social change and by definition, particular applications of technology are vigorously and deliberately pursued for identifiable ends. Its side effects are never at the outset as explicit and usually considered less injurious as its benefits. In other words, it is like a good many therapeutic drugs. The end is identifiable, the side effects less easily anticipated and it is sometimes resolved to put up with them for the sake of benefits of the principal objective. Most of the side effects of technology of which people complain have just this characteristic. How many of us would choose to get rid of air pollution for example by preventing the use of fuel. Aircraft noise is an increasing nuisance, but the quality of life as it is called would be severely damaged by preventing the flight of modern aircraft. The problem of technology then is not that of eliminating side effects but rather of arranging so that their threat to life's quality are so reduced as to make them tolerable.

One of the problems is that in practice the benefits and the side effects are often incommensurable. Another is that the direct benefits of new developments in technology are usually a different group from those most affected by the side effects. For example airlines benefit most obviously from using landing strips in metropolitan areas. Ordinary people are the ones most conscious of the noise. Industrialists benefit most directly from freedom to pollute rivers and lakes while other people are in the process denied the freedom to use the same rivers for other purposes. Some people benefit indirectly from industry's presence in a community

but that is no reason why they should willingly swim in polluted waters or even give up swimming altogether.

In the broadest sense conflicts like these are political conflicts and the question is how the community at large shall regulate the activities of small sections within it. From this point of view the problem of how to prevent despoliation of the environment is ancient history replete with examples of how society retrained commercial interests of the community. Child labor laws is an example of this spirit. A nuisance which goes unresolved in one decade can become intolerable in the next. This is what is happening in air pollution in many advanced societies. It is inevitable, however, that governments with their vested interests will try to conceal awkward conflicts between sections of the community that are not politically aligned in the party and should seem complacent and even malevolent when it comes to caring for the environment.

The community must therefore look to the law and administration for means of controlling the damage done to the environment. To many it seems somewhat of a puzzle that governments should have been allowed to be as lax as they have in matters such as food additives, air and water pollution and therapeutic drugs. Cases like these are best dealt with by means of rigorous laws on innovations when the commercial interests concerned have been able to demonstrate that no unacceptable amount of damage will be done. In this country a fine example is requiring pharmaceutical firms to demonstrate that new drugs should be allowed only where their benefits clearly outweigh any potential damage.

More serious problems arise when it is necessary to strike a balance between social benefit and social damage, such as the building of urban motorways or siting of airfields. This is where the interests of government most frequently conflict with those of the community which they are supposed to serve. The natural and long term corrective is somehow to work out schemes for compensating in money the people most immediately affected by avoidable nuisances. For example industry might be assisted in establishing waste disposal that would not damage our rivers.

But what if the victims of a nuisance are not easily identifiable? Or what if the whole community is affected such as use of organo chlorine insecticides which are a particular problem because of their longevity and ubiquity. Conservationists in their fight against pollution should have clearly in mind the economic value of fertilizers as well as

their hazards, then they might be persuaded to think of schemes for reducing the uses of fertilizers whose nitrates run off into lakes and rivers, but also of schemes for removing the nitrates from lake waters in substantial amounts which might be much cheaper. Pursuit of biological methods for fighting pests is already quite advanced by our Department of Agriculture and may be one way to reduce the use of long lived insecticides.

There is certainly a need of voluntary pressure on governments for this is a political matter. It is important that the pressure groups that are emerging should be hard-headed, dedicated, able to welcome innovation and knowledgeable of side effects these produce. They must pursue both enforcement of laws and carefully watch administrative agencies who are working not for the community but for private interests whom they are supposed to regulate.

The record of the past century shows how technology has prospered and how the quality of life has in the process improved. There is no reason why the same should not happen in the decades ahead if governments recognize their obligation to the people, and the people watch their governments carefully to make sure the common interest receives greater attention than private interests, when these two are in conflict.

L.H.N.

Cellular Immunity In Infectious Disease: The Cellular Mediated Immune Response CMI

Defense mechanisms against infectious agents were thought at one time to rely mainly on bactericidal factors and opsonins. In recent years a second type of defense has come into prominence, the cellular mediated immune response (CMI). Examples of the first method were first explored although Metchnikoff as far back as 1905 insisted on the cellular aspect of immunity.

Some bacteria such as gram negative bacilli are killed directly by serum. Serum was also found to have power to increase the phagocytosis of gram positive cocci and thus to eliminate them from the circulation. Both the serum bactericidal agents and opsonins behaved as typical immunologic agents or antibodies whose concentration increased after exposure to the infective agent whether it was in the form of disease or a vaccine. Protection against infectious diseases such as typhoid or cholera by

vaccinations was found to be associated with an increase in the concentration of specific bactericidal agents or antibodies in the serum. Similarly injection of serum containing antibodies against pneumococci would influence the course of pneumococcal pneumonia and antibodies against diphtheria toxin or tetanus toxin would protect the body from the toxemia of both these agents. The antibodies were found to be gammaglobulin molecules which could be isolated in a pure state and characterized chemically.

Not all infections can be prevented or cured by immune serums however. For example protection against the tubercle bacillus could not be transferred with serum in the same way as protection against the pneumococcus. Moreover infection with the tubercle bacillus leads to a state of skin hypersensitivity which had the peculiar property of taking 24-48 hours to develop a red indurated reaction in the skin. This is quite different from the anaphylactic reaction which take 15-20 minutes to develop. Another form of delayed hypersensitivity is contact sensitivity to simple chemicals which bind the skin surface and converts the subjects own skin into a foreign antigen.

Delayed or contact sensitivity cannot be transferred from one subject to another in the same way as anaphylactic sensitivity but can be transferred from animal to animal by suspensions of mononuclear cells obtained from sensitized donors. An immune process such as that involved in delayed hypersensitivity is involved in homograft rejection. The process underlying delayed hypersensitivity can be shown to play a part in a whole range of immunological processes to which might be added auto-immune states and the defense mechanisms of the body which control the rapid dissemination of cancer.

Since 1967, this aspect of the immune response has been generally referred to as cellular mediated immunity (CMI)² to distinguish it from humoral antibody response. CMI involves the direct interaction of antigen with "specifically sensitized" lymphocytes as a result of which macrophages are activated. It is now realized that CMI accounts for a considerable part of the body's immune reactions in which classical immunoglobulins seem to play no role. It is also significant that CMI is under the control of the thymus in early life since it is not present in neonatal thymectomized animals.

A classical example of CMI in the control of infections has been brought out more strongly by studies of babies born with congenital aplasia of

the thymus. Their serum antibody producing mechanism is intact. They have normal levels of circulating immunoglobulins but survive at most one year since they are susceptible to a wide range of infections. There are other babies born with a congenital defect who cannot synthesize immunoglobulins but have a good level of CMI. These survive into middle childhood. Obviously we need both mechanisms to survive a normal life span.

The infants deficient in CMI cannot be sensitized and do not reject skin grafts. The infants who cannot synthesize immunoglobulins can't cope with pyogenic infections but can resist viral infections such as measles, mumps, varicella and rubella in the normal way. They reject homografts, develop delayed hypersensitivity to tuberculosis, leprosy and certain chemicals. CMI appears to play a major part in the defense mechanisms of the body against most viruses, fungi, protozoa and mycobacteria and also against certain bacterial infections such as *Brucella*, *Salmonella* and *Listeria*.

If CMI is depressed then experimental animals can be infected with leprosy. This also occurs in those humans with a general deficiency in CMI. Conceivably therefore a primary inability of the cellular immune mechanisms allow the infective agent to gain a foothold in the tissues. It must be noted also that it is the lymphocyte whose role is primary for in deficiency of CMI there is an impairment of lymphocyte function. These cells seem to lose their ability to be transformed into blast cells in culture media.

In the next few years we may expect a pure precise definition of the role of CMI in other infectious diseases. The role of CMI in infectious diseases presents a fascinating area in which the immune response can be suppressed both specifically and non-specifically. The relative effects of specific and non-specific suppression of CMI in the course of any particular disease needs now to be assessed very carefully for they will be found to differ from disease to disease.

Many of the clinical manifestations of infectious diseases may turn out to be the direct result of the damaging effects of immune complexes formed in the tissues between humoral antibodies and soluble products of infectious organisms, under conditions where the ability of the body to eliminate the organism by cell-mediated immune responses is impaired. In other diseases such as tuberculoid leprosy and cutaneous leishmaniosis the lesion may be the result of local tissue damage caused by a strong cell mediated reaction against the organism.

We are evidently at the threshold of a further insight into infectious auto-immune diseases, transplant rejection and even the spread of cancer.

L.H.N.

References

1. Cellular immunity in infectious diseases. *Lancet*, II: 253, 1969.
2. *British Med. Bull.*, 23: 1, 1967.

Studies In Human Ecology: Lead Poisoning

Lead poisoning was once an occupational disease. Painters who worked with leaded paint were poisoned, so were devotees of moonshine liquor. So was the bartender whose beer was cooled in lead coils and who took the first draft in the morning. Then, of course, there was the occasional curious child. Now lead as a health hazard has come under increasing scrutiny. New York City once averaged 500 cases of lead poisoning a year. The City Health Department now estimates that a "silent epidemic" of lead contamination may be affecting as much as 25,000 slum children who pick the lead from chipping leaded paint in old buildings. Such lead poisoning has given rise to local political skirmishes and demands for increasing federal regulation and aid.

We know the clinical picture of lead poisoning once enough lead has accumulated in the system. There is a high blood content of lead, convulsions, anemia, vomiting, cramps and symptoms that can be confused readily with those of other less dangerous illnesses if the physician is not looking specifically for lead and his index of suspicion is low. In severe cases, the bone marrow and the central nervous system can be so severely damaged that death or mental retardation can result. Since lead accumulates slowly over a period of months or years, a child can carry a dangerously high level of lead without exhibiting any of the external symptoms.

No one is quite certain how widespread lead poisoning is, but the number of United States children with abnormally high levels of lead may be as high as 225,000. We know how they accumulate this lead. They eat non-food objects such as chips of leaded paint even when they are not hungry. This phenomenon is known as "pica," a reference to the magpie and its indiscriminate eating habits. Since 1940, leaded paint has been replaced by cheaper titanium dioxide-based paints and many localities have banned the use of leaded paints for interior

surfaces. But in some older cities where in the poorer sections many house walls have peeling coats of old leaded paint several studies have indicated that some 5-10 per cent of children between the ages 1-6 have abnormally high blood levels of lead.

The cause is well known and the treatment is equally well established. Once a lead poisoning case is detected the child is hospitalized usually for several days and treated with chelating agents such as BAL and EDTA which bind the lead and remove it from the body. Before chelation therapy was developed 66 per cent of severe lead poisoning cases were fatal. However, with early detection and treatment this figure is down to less than 5 per cent. But of the survivors, brain damage still occurs in more than 25 per cent of the children. When the children come home unhappily they often resume their paint eating habits and if they come down again with lead poisoning the risk of permanent brain damage increases to virtually 100 per cent. They become complete vegetables said Professor of Pediatrics of New York Downstate Medical Center, Hyman Merenstein. It is obvious no child should live in an atmosphere pervaded by lead, nor should he return to such an environment after treatment.

During his lifetime a severely retarded individual can cost health agencies \$250,000 in special training and custodial care Merenstein said. "The horror of it is that lead poisoning is a completely preventable disease. When we used to have 10 polio cases the whole city rose up in arms, but when 30,000 kids are affected with lead poisoning no one notices it."

The long term solution of the problem is to remove leaded paint or to replace the houses. If paint is removed it often does not include removal from the ceiling or upper walls social workers tell us. The real problem then boils down to the will to eradicate this social evil and the money with which to do it. In New York City several rent strikes have been organized after a lead poisoning incident. Wendel O. Rickel, coordinator of a lead detection project near New York stated it this way. "Since the city is not about to enforce the rules, the citizens have to take it upon themselves." Such rent strikes can be particularly successful. Unfortunately the poisoning has to occur first before protest is instituted.

As a stop-gap measure several communities have launched screening programs to detect lead early in young children. In Chicago the City Board of Health has creened over 100,000 children since 1966. Henrietta Sachs, director of the lead poisoning

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Dosage: One or two tablets (well chewed or allowed to dissolve in the mouth); one or two teaspoonfuls to be taken between meals and at bedtime, or as directed by physician.

References: 1. Danhof, I. E.: Report on file. 2. Hoon, J. R.: Arch. Surg. 93:467 (Sept.) 1966.

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clinic said that the number of high levels detected had dropped by roughly a half during each year of the program and the cases detected were less severe. By contrast the New York City Health Department tested blood samples from only 5,000 children last year and these were referrals from city hospitals and clinics and not children tested as a result of an extensive neighborhood screening program. It is obvious that the city is moving too slowly to establish a screening program and in fact community health groups have complained. Inspection of buildings for lead seems even further away.

On the federal level the same inertia is evident. Nineteen Congressmen have submitted a series of 3 bills to provide federal aid for testing programs and assistance in eliminating peeling paint from ghetto dwellings. The bills have not been scheduled for committee action and have received little general support. Community leaders, therefore, will have to deal with the problem within the present legal framework. There is an Environmental Defense Fund that resorts to the courts for relief against degradation of our environment. It is conceivable that this may be one way to demand redress against poisoning in the home.

At a national conference on lead poisoning sponsored by the Scientists Committee for Public Information and other groups Rene J. Dubos of Rockefeller University put it eloquently. He said that "the problem is so well defined, so neatly packaged with both causes and cures known, that if we don't eliminate this social crime, our society deserves all the disasters that have been forecast for it."

L.H.N.

Reference

1. Oberle, M. W.: Lead poisoning: a preventable childhood disease of the slums. *Science*, 165: 991, September 5, 1969.

The First Recorded Case Of Multiple Myeloma

"Mr. M-----, a highly respectable tradesman, aged 45" was the first patient to be described with proven multiple myeloma. William MacIntyre, Thomas Watson, Henry Bence-Jones, and John Dalrymple all participated in the case, and the above quotation is from MacIntyre's paper published in 1850.¹

The patient was under the care of Watson for several months for severe bone pain, and was seen in consultation by MacIntyre on Oct. 20, 1845. Although Watson had not done a urinalysis, Mac-

Intyre noted the presence of a peculiar protein in the urine which dissolved with heating and re-coagulated upon cooling. Both physicians independently submitted specimens of the patient's urine to Bence-Jones, who although only 31 years of age had already established a reputation as a chemical pathologist. He confirmed MacIntyre's findings, studied the protein more extensively, and published three papers describing its nature in 1847 and 1848. The autopsy was performed by Alexander Shaw, but material from two lumbar vertebrae and a rib was submitted to John Dalrymple, and it was he who described the characteristic histological appearance of the lesions.

Mr. M had been well until age 44, when he took a walking tour through the English countryside as a vacation from family and business worries. While exploring a cave, he jumped from the opening and was seized with severe pain in the chest and shoulders. These continued and soon thereafter pain in the flanks and pelvis appeared. He was treated by an anonymous surgeon with bleeding, cupping, leeches, and blisters, and after each bleeding developed a period of exhaustion which would last for many weeks. After coming under the care of Watson and MacIntyre he was given pain-relieving medication and obtained sufficient relief to be able to undertake a walking tour in Scotland. However, he soon developed vomiting and diarrhea, and with these a recurrence of all his previous pains as well as new ones in the back and neck. Further treatment was of no avail, and he died on Jan. 1, 1846, seventeen months after the first symptoms.

The autopsy was attended by all the physicians involved, and they concluded that the disease was "essentially malignant, but different from the true malignant disease of bone, . . . and displaying a set of novel and remarkable reactions which seem to bespeak the existence of some special disease."¹

In 1967 Clamp² traced the identity of Mr. M from details in the papers of MacIntyre and Bence-Jones and a study of the British Register of Deaths. From MacIntyre's paper he learned that Mr. M was a London tradesman, aged 45, who had married early, had numerous children, and had taken the aforementioned holiday in Scotland. Bence-Jones specified that he had been a grocer. Clamp found only one man whose last name began with M, was 45 years old, and died in London on Jan. 1, 1846. He was a grocer named Thomas Alexander McBean, and the cause of death was certified as "atrophy from albuminuria." Other details of McBean's life coincided with the facts concerning Mr. M.

Bence-Jones achieved eponymic fame because of his studies of the protein, although the essential features had already been observed by MacIntyre before the first specimens were submitted to Bence-Jones. MacIntyre died in 1857, but Watson went on to become a baronet, Physician-in-Ordinary to the Queen, and a President of the Royal College of Physicians. His lectures at King's College were published under the title "Principles and Practice of Physic," and earned him comparison with Sydenham and the title of the "British Cicero."

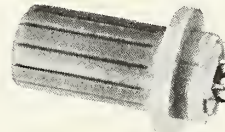
H.L.

References

1. MacIntyre, William, "Case of Mollities and Fragilitas Ossium, Associated with Urine Strongly Charged with Animal Matter, Med-chir. Trans., 33: 211, 1850. Cited by Hayward, Oliver S., "Multiple Myeloma, A Doctor's Disease", Modern Medicine, 196, Aug. 3, 1964.
2. Clamp, John R., "Some Aspects of the First Recorded Case of Multiple Myeloma", Lancet II: 1354, 1967.

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Foreword

The remarkable technical developments in surgery during the past decade have been paralleled by significant advances in diagnostic radiology. In part, the latter were sparked by the demands generated by the new surgical frontiers. However, creative, imaginative radiologic research has provided its own rich harvest.

As a result, there are now available excellent preoperative radiologic techniques for determining the precise locus and etiology of obstructive jaundice, gastrointestinal bleeding and hyperadrenocortical states, the exact organ localization of various intra and extra-abdominal masses including parathyroid adenomas and, to a less satisfactory degree, pancreatic lesions.

In view of these accomplishments, the surgeon has every right to expect his radiologic colleagues in the hospital to utilize the broad armamentarium of radiologic tools available and to choose the technique best suited to the problem at hand. The surgeon also has the right to expect his radiologic colleagues to possess an advanced degree of skill in applying these techniques and an eagerness to cooperate in the workup of problem patients any time of the day or night. The goal must be the highest quality of medical care!

The restrictions imposed by the size of *Connecticut Medicine* preclude a complete discussion of all of the newer advances in diagnostic radiology. The editor has necessarily been compelled to exercise poetic license, so to speak. This has resulted in a number of omissions, not the least of which have been the great contributions of nuclear medicine.

There is every reason to believe that radiology's brilliant achievements will continue to meet the future challenges hurled by its sister surgical specialty. Hopefully, among other developments, this will ultimately lead to the discovery of a method for radio-opacification of the pancreas, the major research interest of the guest editor.

I would be remiss if I failed to express my appreciation to the authors who participated in this issue for their wholehearted cooperation and the excellence of their presentations.

ROBERT SHAPIRO, M.D., *Guest Editor*

Adrenal vein catheterization has three advantages over aortography in the study of pheochromocytoma:

a) direct confirmation of elevated catecholamine levels from the tumor site.

b) no dangerous elevation of blood pressure during the injection of contrast media.

c) no post-catheterization bleeding or hematoma.

I would hasten to add that in most cases aortography and adrenal phlebography are complementary studies and should be done simultaneously. This case presentation is of course unusual in that the mine VMA was consistently normal.

Case 2 This 40 year old negro male was found to have renal tuberculosis because of right renal caliectasis and repeated positive urine cultures for *M. tuberculosis*. A large calcified lesion was noted in the left suprarenal area and assumed to represent calcification of the adrenal gland (Fig. 2). In the course of an angiographic study, the adrenal phlebogram was however found to be normal, and as a result the calcification relegated to a retro-peritoneal lymph node.

We have studied many such examples of shadows or masses in the left upper quadrant which are usually seen on a plain film of the abdomen. The question of whether this is an adrenal mass can be very quickly resolved by adrenal phlebography.



Figure 2

Normal left adrenal vein is unaffected by round calcified mass.



Figure 3

Grapelike pattern of intraglandular venules caused by metastatic deposits within the left adrenal.

Case 3 This 65 year old white male was admitted because of weight loss, pleural effusion and abdominal pain. Because carcinoma of the pancreas was suspected an exploratory abdominal angiogram was requested. The study was non-contributory except for marked distortion of the left adrenal phlebographic pattern which suggested metastatic disease (Fig. 3). Subsequently the patient was found to have a bronchogenic carcinoma and at autopsy, metastatic disease to the left adrenal gland was indeed found.

Metastatic disease to the adrenal gland is commonly found at autopsy in patients with bronchogenic and breast carcinoma. We are currently studying the reliability of adrenal phlebography in the diagnosis of metastatic disease and hope that this can become a useful tool in the preoperative staging of these malignancies.

Conclusion

Selective adrenal phlebography is a simple angiographic procedure which is useful in the evaluation and study of primary adrenal tumors. Its role in the diagnosis of metastatic disease is currently under study.

References

1. Cope, C., Isard, H. J. & Wesolowski, W. E.: Selective adrenal phlebography. *Radiology* 90: 1105-1112, June 1968.
2. Cope, C.: A new one-catheter torque guide system for percutaneous exploratory abdominal angiography. *Radiology* 92:174-175, Jan. 1969.

Angiography In The Diagnosis of Liver Disease

James J. Pollard, M.D., Donald J. Fleischli, M.D. and Robert A. Nebesar, M.D.

Abdominal angiography was initiated in 1929 by Dos Santos, Lamas and Pereira Caldas¹ with a description of translumbar aortography. Although this method was satisfactory for delineation of the abdominal aorta and evaluation of gross abnormalities of its major branches, it did not attain wide use for several years. A method utilizing a catheter placed via an arterial cutdown, introduced by Farinas² in 1941, resulted in some improvement of the quality of the aortogram. Percutaneous catheter introduction via the femoral artery, as first performed by Seldinger³ in 1953, simplified the technique. Odman⁴, using Seldinger's percutaneous technique, achieved selective catheterization of branches of the abdominal aorta, as reported in 1956.

Application of angiographic procedures in obtaining earlier and more accurate diagnosis of diseases of the liver as based on experience at the Massachusetts General Hospital will be presented and illustrated.

Method and Techniques

Angiographic procedures are performed in the Department of Radiology by a radiologist. The percutaneous Seldinger technique of catheter introduction is utilized. The skin and perivascular tissues are anesthetized with procaine, and percutaneous puncture of a vessel of an extremity (usually the femoral artery) is made with a special needle.⁵ A flexible wire, which subsequently serves as a guide for the catheter, is inserted into the artery through the needle which is then removed. A catheter is passed over the indwelling guide wire into the arterial lumen. Once the catheter is well situated within the aorta, the wire is withdrawn. The tip of the catheter is placed into the celiac artery or one of its branches, or into the superior

mesenteric artery under televised fluoroscopic control, and contrast medium, usually methylglucamine diatrizoate (Renografin®), is injected under pressure. A pressure injection results in rapid delivery of a bolus of contrast agent, insuring good concentration. With a selective catheterization only the branch artery and the organ (or organs) that it supplies are opacified when contrast medium is injected. The overlap of other branches of the aorta, which is a drawback of an aortic injection, is eliminated. A larger dose of contrast medium can safely be given to individual viscera resulting in better visceral opacification, since toxicity to the spinal cord and kidneys limits the amount that can be given by an aortic injection. Radiographs are obtained on a rapid serial film changer to record the arterial, capillary (parenchymal) and venous phases of opacification.

In the hands of experienced angiologists the rate of serious complications can now be kept at about 0.5 per cent,⁶ but the ever present possibility of complications dictates that angiography should not be performed except by or under the direction of an experienced angiologist. Similarly, angiography should not be done in a hospital where a vascular surgeon is not available to treat any complications that may arise.

Selective hepatic arteriography is by far the most useful current method for roentgenologic study of the liver. The nature of a hepatic mass can be predicted by arteriography in most cases because of characteristic vascular changes. Arteriography is also useful before an attempt at hepatic resection because the relation of the mass to the hepatic arteries is delineated. Such a specific prediction of the type of mass present and of the anatomic location of the mass is not possible with scanning or any other preoperative means of detection. In addition to showing primary and secondary neoplasm in the liver, arteriography can accurately demonstrate arterial malformations, aneurysms, arterio-

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venous fistulas, hemangiomas, cysts or hepatic trauma.

The accuracy of the arteriographic and isotopic methods of detecting liver abscesses is about equal.^{7, 8} In our early published experience with hepatic arteriography over 70 per cent of neoplastic masses were shown, and false-positive interpretations were relatively uncommon (two of 26 positive interpretations).⁷ Our later unpublished experience with approximately twice as many cases shows a decrease in the number of false-positive interpretations. Liver scanning can detect the masses in about three fourths of the cases of hepatic tumor and the frequency of false-positive interpretations has been reported at 2.5 to 17 per cent.^{9, 10} Blind needle biopsy is reported to be 70 to 80 per cent accurate in the detection of tumor within the liver.¹¹

Preliminary routine screening for hepatic masses is best performed by isotopic scanning because it is simpler, safer, and cheaper than angiography. Arteriography is indicated before hepatic surgery, when more specific information is desired, or when a scan is equivocal. Angiography and scanning are complementary—for example, when a normal scan may allow questionable angiographic abnormalities to be ignored or vice versa (in such a case the angiographic abnormalities are usually due to normal variations of the intrahepatic vascular pattern).

The anatomy of the hepatic arteries, so basic to correct angiographic diagnosis, is thoroughly described in a recently published text.¹² Of particular note is the frequent aberrant origin of hepatic arteries. The most common aberrant origins are a right hepatic artery arising from the superior mesenteric artery in 16 per cent and a left hepatic artery arising from the left gastric artery in 18 per cent of cases. These aberrant arteries are important surgically since they are the sole supply to the hepatic segment that they serve. When perflusion of the liver for diffuse tumor is attempted, such arterial variants must be excluded,^{12, 13} lest a catheter in the common hepatic artery leave a large volume of tumor containing liver untreated. A complete angiographic study of the liver must include opacification of all the hepatic arteries.

Primary Hepatic Neoplasms

Arteriographically, hepatomas in both adults and children are quite distinctive in appearance and almost all can be detected^{7, 14-16} (Fig. 1). They usually are easily recognized by the enlarged hepatic arteries feeding many irregular tumor vessels either within a single large hepatic mass or within mul-



Figure 1

Selective Celiac Angiogram Showing a Large Hepatoma (Single-tailed Arrows) in the Lower Part of the Right Lobe of the Liver. The tumor is fed by enlarged intrahepatic arteries and contains numerous tumor vessels. Because of the vascularity of the hepatoma blood is preferentially shunted through it as manifested by the more attenuated intrahepatic arteries in the normal part of the right lobe (double-tailed arrow). (Reprinted from Pollard and Nebesari¹⁴ with the permission of the publisher).

iple smaller nodules. Arteriovenous shunting may or may not be present. These tumors almost always show a dense tumor stain, and the rate of flow of contrast medium through them varies. Infrequently, a hepatoma may be relatively avascular, and, if it outgrows its blood supply, it may become necrotic. (Fig. 2) Portal vein obstruction and evidence of hepatic vein obstruction may be detected during the venous phase of celiac and superior mesenteric arteriography as the contrast medium drains from the spleen or gut wall to fill the portal venous system.

Cholangiocarcinoma is difficult to detect angiographically because it is avascular and may cause very little vessel displacement.⁷ It may, however, narrow or obstruct hepatic arteries¹⁴—a relatively rare finding with most hepatic cancers.

Hamartomas contain varying degrees of small-vessel proliferation. Therefore, some appear avascular on angiography⁷, and others are vascular.¹⁵ A liver-cell adenoma was reported which showed both moderately vascular and relatively avascular areas.¹⁹

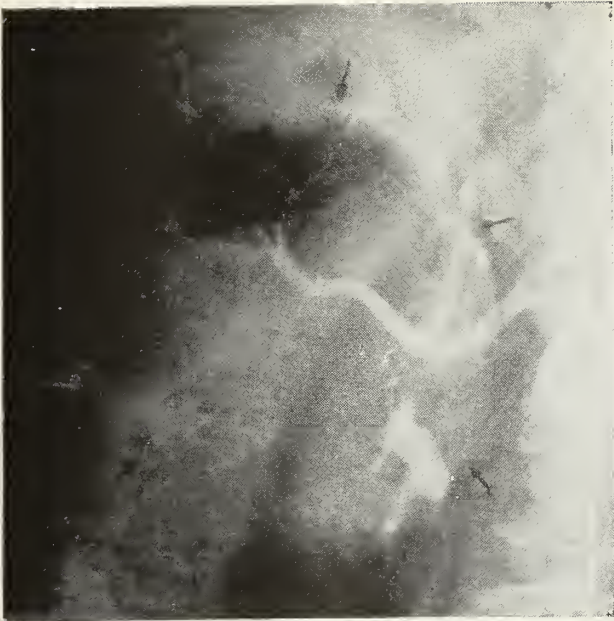


Figure 2

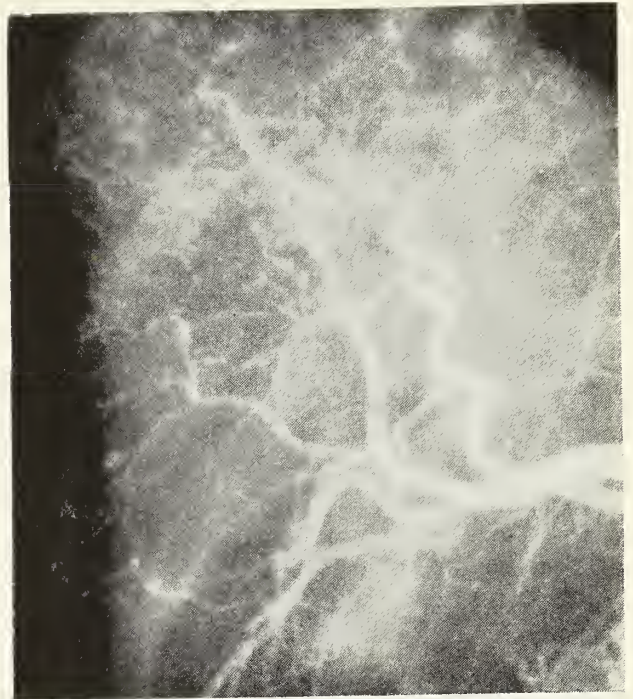
Necrotic mass thought at laparotomy to be hepatic abscess was drained. Angiogram discloses displaced arteries surrounding the mass with gas within. Margins of the mass (arrows) show small irregular vessels with stain characteristic of tumor. (Biopsy performed on basis of angiographic findings disclosed necrotic hepatoma). (Reproduced from Nebesar *et al.*⁷ with the permission of the publisher).

Since hemangiomas are extremely vascular, they are readily detected by angiography. Some believe that they are difficult to differentiate from hepatoma or other lesions,²⁰ but it is our opinion that certain characteristic features allow differentiation from hepatoma in most cases. Unlike hepatomas, they have very small feeding arteries. These fill very large irregular sinusoidal spaces, which retain contrast medium for as long as 20 seconds or more.²¹ (Fig. 3) These features of extremely slow flow, small feeding vessels and stagnation within large sinusoids are seldom encountered in most other hepatic tumors. The hemangioendothelioma of infancy, on the other hand, shows very rapid flow through large hepatic arteries; clinically, it often presents as massive arteriovenous shunting with congestive heart failure.^{22, 23}

Hepatic Metastases

Carcinoma metastatic to the liver is much more common than primary lesions since 35 to 50 per cent of all neoplasms metastasize to the liver.¹¹ Some hepatic metastases are less vascular than the surrounding normal liver and thus appear as filling defects during the arterial hepatogram phase. These avascular appearing metastases are difficult

Figure 3



A. Arterial phase of celiac artery injection showing beginning filling of hemangioma in upper lateral portion of the right lobe of the liver.



B. Several seconds later. There is persistence of contrast medium in the sinusoids of the hemangioma. (Reproduced from Pollard *et al.*²¹ with the permission of the publisher).

to detect. If avascular lesions are large, they may cause displacement of the intrahepatic arteries. Vessel displacement and defects in the arterial hepatogram are nonspecific signs and indicate only that masses are present within the liver; similar changes can be seen with other masses such as abscesses, cysts, hematomas and so forth.

With diffuse replacement of the liver by small, relatively avascular metastases, diagnosis may be difficult. The liver shows stretching of hepatic arteries without their displacement, and the arterial hepatogram shows only a mottled appearance. These findings are nonspecific; identical findings are seen in the precirrhotic stage of alcoholic hepatitis with fatty infiltration, in viral hepatitis, in biliary obstruction, in hepatic-vein obstruction and in any other condition causing hepatic enlargement.

Figure 4



A. Malignant metastatic carcinoid shows slight stretching of liver arteries and many areas of small tumor vessels.



B. Later phase films demonstrate the dense tumor stain of multiple metastatic nodules (confirmed by surgery). (Reproduced from Nebesar *et. al.*⁷ with the permission of the publisher.)

Vascular metastases seem more frequent and occurred in over two-thirds of our cases and thus a definite diagnosis of malignancy could be made in these tumors. The most vascular metastases are leiomyosarcoma, renal-cell carcinoma, malignant carcinoid, and malignant islet-cell tumor. Leiomyosarcoma and renal-cell carcinoma tend to show large tumor vessels whereas the malignant carcinoid and islet-cell tumors show chiefly an intense tumor stain. (Fig. 4) Slight to moderately increased vascularity is often seen in the metastases of adenocarcinoma of the colon, endometrium and breast, as well as in those of carcinoma of the adrenal gland, seminoma and forms of pancreatic carcinoma other than adenocarcinoma. Adenocarcinomas of the stomach, pancreas, bile ducts and gallbladder are usually avascular, as are metastatic lesions from squamous cell carcinoma of the lung and esophagus and Wilm's tumor. These avascular

lesions may rarely cause stenosis or occlusion of intrahepatic arteries. Some tumors, such as melanoma, show variable vascularity.²⁴

The intra-arterial injection of epinephrine immediately before angiography, which is so often helpful in renal lesions^{25, 26} has not, in our hands, helped appreciably in the differentiation of benign and malignant masses of the liver.

Other Liver Diseases

A variety of other diseases affecting the liver can be demonstrated angiographically. Some must be considered in the differential diagnosis of neoplasia, and include inflammatory processes, cirrhosis, regenerating nodules, cysts and hematomas.

An intrahepatic abscess can be accurately shown and differentiated from a subdiaphragmatic abscess. Most intrahepatic abscesses displace hepatic arteries and show, during the arterial hepatogram, a round avascular defect with a surrounding thin halo of hyperemic staining.^{20, 27-29} A more hypervascular appearance, with abnormal-appearing vessels, may be seen in long standing chronic granulating infection.³⁰

Stretching of the intrahepatic arteries (indicating hepatic enlargement) and hypervascularity have been reported in cirrhotic patients with acute alcoholic hepatitis.³¹ This is in contrast to viral hepatitis, which may show stretched arteries that

are small and thin and a hepatogram that is less than normally dense.³²

Morphologic alterations in the liver due to cirrhosis are associated with variable changes in all its blood vessels that reflect the severity, extent, and form of cirrhosis present. In the early stages of cirrhosis, the findings may be few. In the fatty, infiltrative precirrhotic stage, or in hypertrophic cirrhosis, all the vessels may be stretched and narrowed. In the late fibrotic stage of cirrhosis, the hepatic arteries outside the liver may enlarge owing to increased arterial flow and show a corkscrew pattern within the liver. The corkscrew appearance, although seen most frequently in cirrhosis, is a nonspecific finding reflecting loss of liver volume due to parenchymal destruction. The probable explanation of this appearance is as follows: The arteries may be thought of as a scaffolding throughout the liver, which is not destroyed by the cirrhosis, as is the parenchyma. As the destroyed parenchyma shrinks, the arteries buckle upon them-

Figure 6
Polycystic Disease of Liver



Right hepatic artery arises from superior mesenteric artery, which has been injected. Note stretching and curvilinear displacement of intrahepatic arteries around cysts. On another angiogram the left hepatic artery was seen to arise from the celiac axis, and the same pattern of stretching and curvilinear displacement was present in its intrahepatic branches.

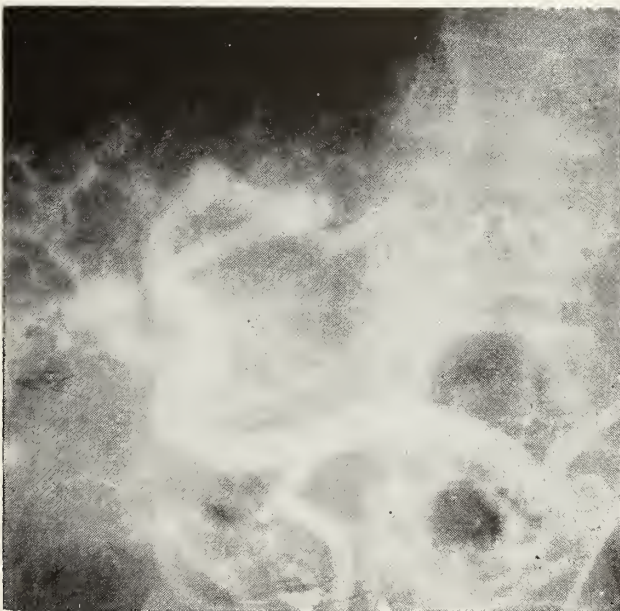


Figure 5

Small chunken cirrhotic liver with a corkscrew appearance of the intrahepatic arteries. Celiac artery injection. (Reproduced from Pollard *et. al.*²¹ with the permission of the publisher).



B. The mottled appearance in the arterial hepatogram phase is caused by avascular cysts superimposed against the density of contrast material in the normal liver tissue. The same pattern was seen in the left lobe of the liver on the angiogram filling the left hepatic artery. (Reproduced from Pollard *et. al.*²¹ with the permission of the publisher).

selves, and thus produce the characteristic corkscrew appearance.²¹ This may be seen in other conditions such as congenital hepatic fibrosis.³³

Cysts of the liver, whether nonparasitic or parasitic, present as avascular masses with displacement and stretching of arteries and sharply defined radiolucency in the hepatogram.^{20, 21, 27} Hydatid cysts have been reported to show, in addition, during the portal venous phase a thin rim of radiopacity due to the passage of contrast material between the hydatid membrane and the pericystic layer.³⁴ In polycystic disease the lesions are several, and the liver is enlarged;²¹ if the kidneys are also involved, similar changes are seen on renal angiography. (Fig. 6)

Hepatic trauma is common, serious and at times difficult to detect before operation. The amount of deep injury may be difficult to ascertain at laparotomy from external inspection of the liver.³⁵ In our experience angiography has been quite valuable in accurately demonstrating the location, nature and extent of the liver injury.³⁶ Subcapsular



Figure 7

Selective Superior Mesenteric Angiogram of a Patient Involved in an Automobile Accident.

Note the chest tube (white arrow) and fractured right lower rib (just above the upper black arrow). Branches of the celiac artery fill via collaterals in the head of the pancreas (not in itself abnormal). Note puddles of contrast medium in the hepatic laceration in the inferolateral aspect of the right lobe of the liver (black arrows). (Reproduced from Pollard and Nebesar²⁴ with the permission of the publisher).

hematoma may be accurately diagnosed. The angiographic signs of hepatic laceration or rupture include displacement and disruption of vessels, localized accumulation of contrast medium in the damaged liver parenchyma, extravasation of contrast material into a bile duct, arteriovenous shunting into the hepatic or portal vein and displacement of the liver or of surrounding viscera.³⁷ (Fig. 7)

Summary

Hepatic angiography provides useful, often definitively diagnostic information concerning liver disease. It has already assumed its place in the diagnostic armamentarium of the radiologist in the teaching hospital and in the progressive community hospital.

References

1. Dos Santos, R., Lamas, C. Pereira Caldas, J.: L'arteriographie des membres de l'aorte et de ses branches abdominales. *Bull Soc Chir Paris* 55:587-601, 1929.
2. Farinas, P. L.: New technique for arteriographic examination of abdominal aorta and its branches. *Amer J Roentgen* 46:641-645, 1941.

3. Seldinger, S. I.: Catheter replacement of the needle in percutaneous arteriography. *Acta Radiol* 39:368-376, 1953.
4. Odman, P.: Percutaneous selective angiography of main branches of the aorta. *Acta Radiol* 45:1-14, 1956.
5. New, P. F. J. and Baker, E.: Technique of arterial puncture. A new needle cannula for arteriography. *J Neurosurg* 20: 390-396, 1963.
6. Lang, E. K. Prevention and treatment of complications following arteriography. *Radiology* 88:950-956, 1967.
7. Nebesar, R. A., Pollard, J. J., and Stone, D. L. Angiographic diagnosis of malignant disease of the liver. *Radiology* 86:284-292, 1966.
8. Georgi, M., Winkel, K., and Pypic, B. Zoliakographie und Szintigraphie in der radiologischen Diagnostik von Lebermetastasen. *Strahlentherapie* 127:405-417, 1965.
9. Gollin, F. F., Sims, J. L. and Cameron, J. R. Liver Scanning and liver function tests: comparative study. *J.A.M.A.* 187:111-116, 1964.
10. Nagler, W., Bender, M. A., and Blau, M. Radioisotope photoscanning of liver. *Gastroenterology* 44:36-43, 1963.
11. Gall, E. A. Tumors of the liver. In *Diseases of Liver: With a Foreword by Cecil J. Watson. Second Edition.* Edited by L. Schiff. Philadelphia: Lippincott, 1963. Pp. 702-727.
12. Nebesar, R. A., Kornblith, P. L., Pollard, J. J. and Michels, N. A. Celiac and Superior Mesenteric Arteries: A correlation of angiograms with dissections. Boston: Little, Brown, 1969.
13. Khazei, A. M. and Watkins, E., Jr. Hepatic artery anomalies or deformities managed during infusion chemotherapy of liver cancer. *S. Clin. North America* 45:639-655, 1965.
14. Boijesen, E., and Abrams, H. L. Roentgenologic diagnosis of primary carcinoma of liver. *Acta radiol. (Diagn.)* 3: 257-277, 1965.
15. Yu, C. Primary carcinoma of liver (hepatoma): its diagnosis by selective celiac arteriography. *Am. J. Roentgenol.* 99: 142-149, 1967.
16. McDonald, P. Hepatic tumors in childhood. *Clin. Radiol.* 18:74-82, 1967.
17. Vaimonte, M., Jr., Ravel, R., Politano, V., and Bridges, B. Angiographic findings in patient with tuberous sclerosis. *Am. J. Roentgenol.* 98:723-733, 1966.
18. Sieberns, H. Rontgenologischer Beitrag zur Diagnose eines Hamartoblastoms der Leber. *Fortschr. a. d. Geb. d. Rontgenstrahlen* 102:586-588, 1965.
19. Palubinskas, A. J., Baldwin, J., and McConmack, K. R. Livercell adenoma: angiographic findings and report of case. *Radiology* 89:444-447, 1967.
20. Boijesen, E. Selective hepatic angiography in primary and secondary tumors of liver. *Rev. internat. hepat.* 15:385-395, 1965.
21. Pollard, J. J., Nebesar, R. A., and Mattoso, L. F. Angiographic diagnosis of benign disease of liver. *Radiology* 86:276-283, 1966.
22. Levick, C. B., and Rubie, J. Haemangioendothelioma of liver simulating congenital heart disease in infant. *Arch. Dis. Childhood* 28:49-51, 1953.
23. DeLorimier, A. A., Simpson, E. B., Baum, R. S., and Carlsson, E. Hepatic-artery ligation for hepatic hemangiomas. *New Eng. J. Med.* 277:333-337, 1967.
24. Pollard, J. J. and Nebesar, R. A. *Medical Progress. Abdominal Angiography.* *New Eng. J. Med.* 279: 1035-1042, 1093-1100, 1148-1152 (November 7, 14 and 21), 1968.
25. Abrams, H. L. Response of neoplastic renal vessels to epinephrine in man. *Radiology* 82:217-224, 1964.
26. Kahn, P. C. Epinephrine effect in selective renal angiography. *Radiology* 85-301-305, 1965.
27. Bosniak, M. A. and Phanthumachinda, P. Value of arteriography in study of hepatic disease. *Am. J. Surg.* 112:348-355, 1966.
28. Urschel, H. C., Jr., Skinner, D. B., and McDermott, W. V., Jr. Hemobilia secondary to liver abscess: report of case treated by partial hepatectomy. *J.A.M.A.* 186:797-799, 1963.
29. Margulis, A. R. Some new approaches to examination of gastrointestinal tract. *Am. J. Roentgenol.* 101:265-286, 1967.
30. Baum, S. Arteriography in diagnosis of abdominal disease. In *Gastroenterology.* Edited by H. L. Bockus et al. Second Edition. 3 vol. Vol. 3. Philadelphia: Saunders, 1965, Pp. 1186-1229.
31. Rourke, J. A., Bosniak, M. A. and Ferris, E. J. Hepatic angiography in "alcoholic hepatitis." *Radiology* 91:290-296, 1968.
32. Evans, J. A. Specialized roentgen diagnostic technics in investigation of abdominal disease: annual oration in memory of Clarence Elton Hufford, 1893-1958. *Radiology* 82:579-594, 1964.
33. Ellis, D. S., and Putschar, W. G. J. Case Records of the Massachusetts General Hospital (Case 16-1968). *New Eng. J. Med.* 278:899-904, 1968.
34. McNulty, J. G. Angiographic manifestations of hydatid disease of liver: report of two cases. *Am. J. Roentgenol.* 102: 380-383, 1968.
35. Mills, R. H. Problems of closed liver injuries. *Gut* 2:267-276, 1961.
36. Ackroyd, F. W., Pollard, J. J. and McDermott, W. V., Jr. Massive hepatic resection in the treatment of severe liver trauma. *The American J. Surg.* 117:442-448, April, 1969.
37. Boijesen, E., Judkins, M. P., and Simay, A. Angiographic diagnosis of hepatic rupture. *Radiology* 86:66-72, 1966.

Hypotonic Duodenography

For Improved Radiologic Evaluation of Pancreaticoduodenal Disease

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Hypotonic duodenography is a simple and effective technique for improving the radiologic diagnosis of pancreatic disease. This paper briefly describes the examination technique, discusses technical details, diagnostic criteria, and summarizes reliability statistics.

Technique

The examination is begun by intubating the duodenum. A commercial unit consisting of a thin-walled polyethylene tube and a separate guide wire is available for this purpose.* The whole unit is maneuvered under fluoroscopic control until the tip of the tube is at the pyloric canal. The guide wire is withdrawn slightly and the flexible tube is passed over it into the duodenum. Its tip is positioned at the junction of the second and third portions, and then the guide wire is withdrawn completely. Sixty mg. of propantheline bromide (Probanthine®) is given intramuscularly. This dose usually produces satisfactory duodenal relaxation within five minutes.

At this point enough barium is administered through the tube to produce duodenal distension. "Spot films" of the barium-filled duodenal loop are made in various projections, barium is aspirated, and the duodenum insufflated with air. This produces a double contrast examination and several additional spot films are obtained. The procedure is relatively simple, requiring an average of 30 minutes for completion.

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Complications

The only significant problems encountered in the 150 cases of our series were a few early instances of urinary retention. These can be prevented by having all elderly male patients void before the study and restricting their fluid intake for several hours after it. There have been no cardiovascular complications and acute glaucoma has not been precipitated.

Interpretation

The duodenogram is an extension of the standard gastrointestinal examination. There are differences, but these simplify analysis. Maximal duodenal distension produces a larger pancreaticoduodenal interface, increasing the likelihood of detecting pancreatic pathology. Duodenal hypotonia and air contrast technique permit a more accurate radiographic analysis of anatomic features than previously possible. Nonetheless, the study is interpreted by application of the same diagnostic criteria used for evaluating conventional upper gastrointestinal examinations.

The normal duodenal loop, as demonstrated by duodenography, is fairly even in caliber, has a regular fold pattern, and gently arcuate borders. (Fig. 1) Along the inner border, folds are fairly uniform in depth and appearance. The normal papilla of Vater is demonstrated occasionally as a smoothly-rounded filling defect no greater than 1.5 cm. in diameter. Actually, the normal papilla is recognized less often than might be expected.

On the other hand, the enlarged duodenal papilla is usually easy to recognize. Figure 2 demon-

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Figure 1
Normal duodenogram. Note the normal papilla (arrow).



Figure 2
Enlarged papilla due to impacted ampullary stone.

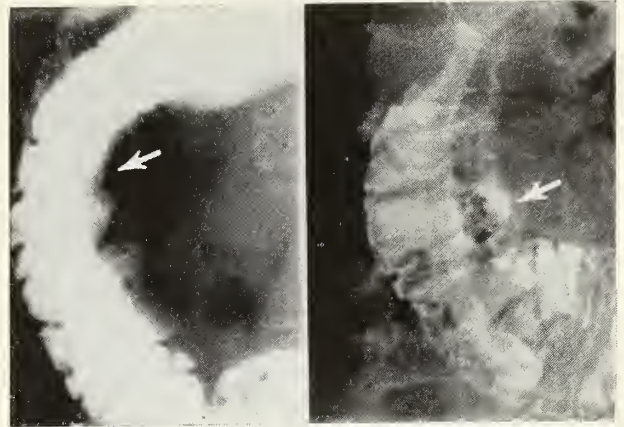


Figure 3a
Spiculation and nodularity in proven pancreatic carcinoma.

Figure 3b
Spiculation in acute pancreatitis.

strates papillary enlargement due to an impacted ampullary stone which usually produces a smooth-surfaced lesion. This appearance is sufficiently characteristic that preoperative diagnosis is frequently possible. Small tumors of the papilla have a similar appearance but are exceedingly rare.

The radiographic features most helpful in identifying carcinoma of the pancreas are "spiculation" with associated nodular indentation of the inner border of the medial duodenal loop. (Fig. 3a) Spiculation consists of finely pointed serration. It appears to occur more commonly in pancreatic cancer, but has also been demonstrated in acute pancreatitis. (Fig. 3b) Fortunately, acute pancreatitis and pancreatic cancer can usually be distinguished on clinical and laboratory grounds. We have not observed spiculation in chronic pancreatitis. In some instances pancreatic carcinoma may be manifested by the classic but nonspecific inverted "3" deformity (Frostberg's sign), or less often by reflux into the ampulla of Vater and common bile duct. Such reflux also occurs in patients who have had prior sphincterotomy.

When only a nodular mass (without spiculation) is present, interpretation is more difficult. If the surface of the lesion is irregular, malignancy is more likely. (Fig. 4a) If the lesion is smooth-surfaced, a benign condition can be suspected. (Fig. 4b) This sort of distinction can be quite subjective. Careful attention to all available clinical information improves diagnostic accuracy. In some instances, both roentgen and clinical manifestations are nonspecific. In these situations definite knowledge that a nodular lesion is present can still be of great clinical importance.



Figure 4a

Proven pancreatic cancer. Note slightly lobulated surface.



Figure 4b

Impacted ampullary stone with smooth enlargement of the papilla.

Straightening of the inner border of the duodenal loop with effacement of the fold pattern is a reliable indicator of chronic pancreatitis. (Fig. 5) It can be seen on either barium-filled or air-contrast views and can be a striking finding. Simple straightening of the contour without fold effacement is a frequent normal finding and should be carefully distinguished from straightening with effacement.¹

Thickened, edematous duodenal folds are a sign of acute inflammation and can occur in acute pancreatitis (where they are occasionally associated with spiculation) and in peptic ulcer disease (e.g. Zollinger-Ellison Syndrome. (Fig. 6)

Although primarily designed for demonstration of the second portion of the duodenum, duodenog-

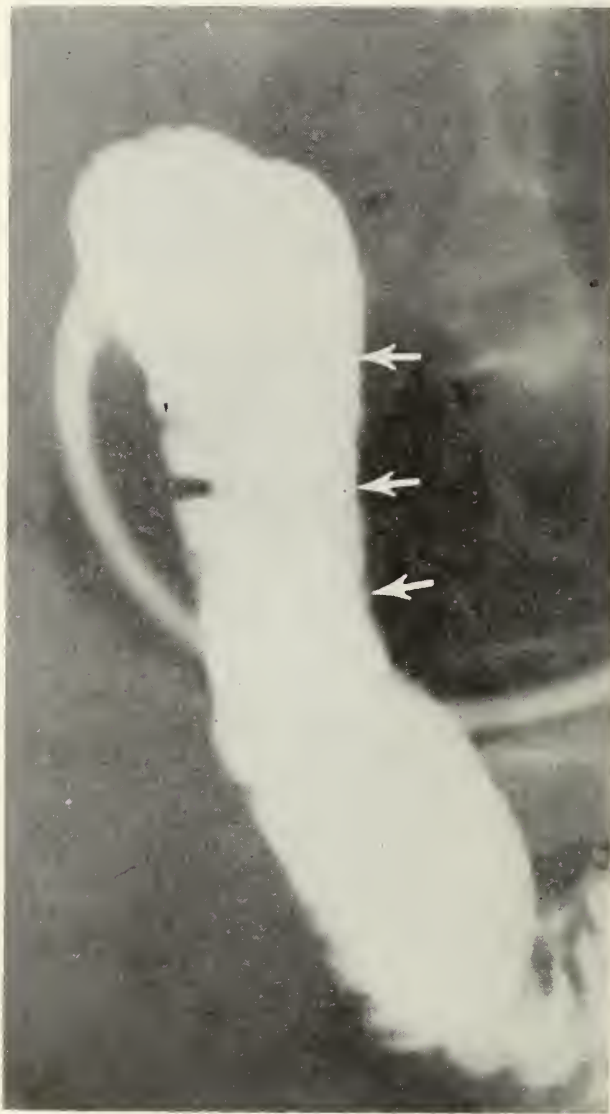


Figure 5a

Straightening with fold effacement (arrows). Chronic pancreatitis.

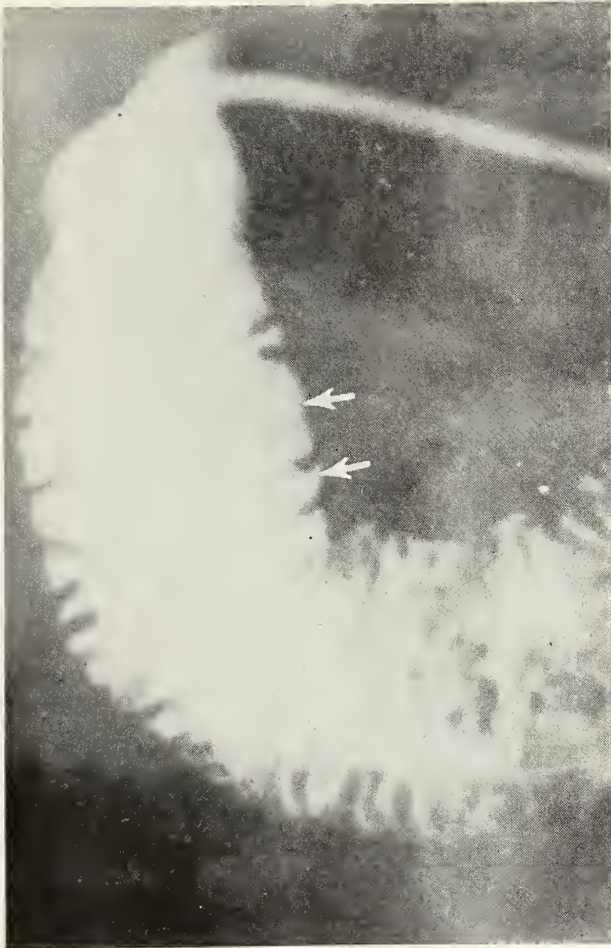


Figure 5b

Straightening without effacement (arrows). Normal case.

raphy can also demonstrate normal distal duodenal anatomy and pathology.¹

In summary, spiculation and flattening have been quite reliable findings; the former for cancer or acute pancreatitis and the latter for chronic pancreatitis. There are, however, some patients whose studies demonstrate nodular indentation without either spiculation or flattening. Although the surface features give suggestive information these findings are really nonspecific and careful correlation with the available clinical data is suggested in such cases. Thickened edematous folds represent a sign of acute inflammation.

Reliability Statistics

A number of published series indicate 20 to 50 percent prospective accuracy in diagnosing lesions in the head of the pancreas by conventional gastrointestinal examination.²⁻⁴ Retrospective accuracy has been higher, ranging from 60 to 75 percent.^{5, 6} A fair average figure for accuracy by conventional

“upper G.I. series” is probably in the 50 percent range. With hypotonic duodenography, prospective data suggests 78 percent⁷ accuracy while retrospective and unspecified estimates range from 75 to 90 percent.^{8, 9} Although none of these series represent a “double-blind” study and hence reflect a certain degree of “bias,” they do demonstrate a higher diagnostic accuracy with duodenal hypotonic examinations.

Conclusions

Hypotonic duodenography is a safe and simple extension of the conventional gastrointestinal roentgen examination. It is designed for optimal demonstration of the duodenum and its intimate relationship to the head of the pancreas. Analysis of available reliability figures indicates that duodenography significantly improves radiologic accuracy in diagnosis of disease in the head of the pancreas.



Figure 6

Mucosal thickening in Zollinger-Ellison Syndrome.

There are two major indications for the procedure. First, all patients suspected clinically of having cancer of the head of the pancreas, ampulla of Vater, or duodenum should have duodenography as part of their "work up." While many of these patients will have lesions demonstrable by conventional examination, the findings can be better shown and clarified by duodenography. In certain cases patients with negative conventional studies will have positive findings on duodenography. Second, many patients in whom no duodenal or pancreatic disease is suspected have equivocal or apparently positive duodenal findings on conventional "G.I. series." Duodenography is an appropriate follow-up exam.¹⁰ The original findings may be confirmed and extended or the duodenum may be shown to be normal. In either case, clinical management is facilitated.

Because of its simplicity, effectiveness, and relatively common indications, hypotonic duodenography should become generally available in the near future. Its widespread utilization should result in improved radiologic diagnosis of pancreaticoduodenal disease.

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References

1. Ferrucci, J. T., Jr., Benedict, K. T., Jr., Fleischli, D. J., and Eaton, S. B.: Hypotonic duodenography: normal and variant duodenal anatomy. In Preparation.
2. Eyster, W. R., Clark, M. D., and Rian, R. L.: Evaluation of roentgen signs of pancreatic enlargement. *JAMA*, 181: 967-971, 1962.
3. Hodes, P. J., Pendergrass, E. P., and Winston, N. J.: Pancreatic, ductal, and vaterian neoplasms: their roentgen manifestations. *Radiology*, 62: 1-15, 1954.
4. Beeler, J. W., and Kirklin, B. R.: Roentgenologic findings accompanying carcinoma of the pancreas. *Amer. J. Roent.*, 67: 576-584, 1952.
5. Broadbent, T. R., and Kernan, H. O.: One hundred cases of carcinoma of the pancreas: clinical and roentgenologic analysis. *Gastroenterology*, 17: 163-177, 1951.
6. McClore, F. B., Robertson, D. S., and Grogan, J. M.: The roentgen manifestations of pancreatic tumors. *Gastroenterology*, 31: 551-565, 1956.
7. Eaton, S. B., Fleischli, D. J., Pollard, J. J., Nebesar, R. A., and Potsaid, M. S.: Comparison of current radiologic approaches to the diagnosis of pancreatic disease. *New England J. Med.*, 279: 289-396, 1968.
8. Jacquement, P., Liotta, D., and Mallet-Guy, P.: The Early Radiological Diagnosis of Disease of the Pancreas and Ampulla of Vater: Elective Exploration of the Ampulla of Vater and the Head of the Pancreas by Hypotonic Duodenography. Springfield, Ill., Charles C. Thomas, 1965.
9. Bilbao, M. K., Rosch, J., Frische, L. H., and Dotter, C. T.: Hypotonic duodenography in the diagnosis of pancreatic disease. *Sem. Roent.*, 3: 280-287, 1968.
10. Benedict, K. T., Jr., Ferrucci, J. T., Jr., Eaton, S. B. and Fleischli, D. J.: Duodenal pseudolesions: role of hypotonic duodenography in defining nature and extent of disease. In Preparation.

SPEECH

He knew the precise psychological moment when to say nothing.—Oscar Wilde

Percutaneous Transhepatic Cholangiography

John A. Evans, M.D. and Zuheir Mujahed, M.D.

The clinical differentiation between jaundice caused by obstructive biliary disease and jaundice caused by destruction of liver cells and impaired liver function can be difficult and at times inconclusive. Competent internists may be unsure of the diagnosis. Chemical laboratory tests may not offer the clear cut information sought by the clinician or they may be ambiguous. Prior to the introduction of percutaneous cholangiography the radiologist was also unable to give his clinical colleagues any help in the matter, as neither oral cholecystography nor intravenous cholangiography could opacify the biliary ducts or gall bladder in jaundiced patients. A serum bilirubin over 3.5 mg. per 100 cc interferes with the excretion by the liver of the oral as well as the intravenous contrast agents. This occasional inability to reach a conclusive differentiation between obstructive jaundice and hepatocellular jaundice is unfortunate. A mistaken diagnosis of an obstructive condition in a patient suffering from a hepatocellular disease will lead to surgical exploration with its high mortality in this group of patients. In the last decade, the use of television fluoroscopy during percutaneous cholangiography has made this a safe, accurate and reliable diagnostic procedure in the jaundiced patient. The examination is helpful when performed by an experienced person on carefully selected patients.

Historical. It is of interest that the percutaneous opacification of the gall bladder preceded the oral and intravenous method. Graham and Cole¹⁻³ published their articles on cholecystography in 1924 and 1925. Four years earlier Burkhardt and Müller⁴ introduced a needle percutaneously into the gall bladder in an attempt to opacify the biliary tree and gall bladder. The examination was performed under local or general anesthesia, and the needle was introduced in the 8th intercostal space, one centimeter anterior to the mid-axillary line. The needle reached the gall bladder after traversing the liver. The method never became popular probably

because of the advent of the more easily performed cholecystography.

Between 1930 and 1952 several investigators, all of them outside the North American continent attempted direct opacification of the biliary tree through the percutaneous introduction of a needle into the liver or the gall bladder. The work of Burkhardt and Müller has already been referred to. In 1937, Huard and Do-Xuan-Hop⁵ introduced Lipiodol percutaneously into the liver and opacified the biliary tree. In 1942 Royer et al⁶ injected the gall bladder with a radiopaque medium under direct visualization at peritoneoscopy.

The credit for first introducing this examination in the North American continent goes to Carter and Saypol⁷ who reported their experience in an issue of the JAMA and stimulated interest in the procedure. Their article was followed by several other articles by various authors.⁸⁻¹²

Various modifications of instruments and techniques have been advocated. One such modification is described by Varela Fuentes⁸ and his associates. In order to improve the chances of encountering a bile duct of adequate size within the liver they used a needle with six perforations on the side. Hanafee and Weiner¹³ described an alternate method of reaching the biliary system. They passed a catheter percutaneously via the right internal jugular vein and directed it into the superior vena cava, right atrium, and inferior vena cava. Through this catheter a needle was inserted for the puncture of the biliary system inside the liver. They performed the procedure on 11 patients.

Procedure. Before the examination is performed the patient's clotting mechanism should be determined and a bleeding tendency ruled out. The procedure is restricted to patients scheduled for surgery and is performed an hour or two before the operation. The premedication is the same as that given for the planned laparotomy. It usually consists of 130 mg. of Phenobarbital and 100 mg. of Demerol intramuscularly one hour before the examination. The cholangiogram is performed in the radiology department with a television screen to monitor the insertion of the needle in the liver.

Recent technical improvements especially the marketing of a portable radiographic unit with a television screen allows the performance of per-

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cutaneous cholangiography in the operating room prior to exploration. Whether in the operating room or in the radiology department the procedure is performed by the radiologist. He alone is familiar with the use of the equipment and he alone is involved in every examination and can therefore acquire enough technical skill and experience in the performance of the procedure.

The skin over the chest and upper abdomen on the right side is prepared and draped. The site of injection is infiltrated with 1 percent procaine. The patient is instructed to avoid deep breathing during the procedure. A 7 inch, 20 or 21 gauge needle with a stylet is introduced into the skin, below the costal margin in the midclavicular line and advanced through the abdominal wall into the liver. The needle is held at an angle of 45° with the skin, and directed medially. As the needle enters the liver a characteristic sensation of varied resistance is obtained. The stylet is then removed and a 20 cc syringe with a polyethylene tubing is joined to the needle. As the needle is advanced into the liver parenchyma aspiration by gentle withdrawal of the plunger is carried out until bile is freely obtained. The syringe is replaced with another one containing 10 to 20 cc of 75 percent Hypaque. Hypaque is then injected slowly, the process being monitored on the television screen. The procedure is much easier and more likely to be successful if the intrahepatic biliary system is dilated. In a previous article (12) we reported a 92 percent success if the bile ducts were dilated as against only 43 percent when the ducts were not dilated. The overall success rate was 74%. This is in general agreement with the findings of other authors.¹⁴

If no bile duct is encountered by the needle as it is first inserted and there is no immediate bile flow, the needle is inserted further into the liver substance under television observation. Small amounts of 1.0 to 2.0 cc of contrast agent are injected as the needle is inserted. An injection into a bile duct is indicated by the filling of branching channels into which the contrast material collects and moves very slowly. An injection into a vein or an artery is recognized by the quick disappearance of the contrast agent as it is carried away by the blood stream. An irregular, stagnant puddle of contrast agent denotes injection into the liver parenchyma. When filling of the biliary tree has been accomplished the needle is withdrawn and radiographs are taken.

If biliary decompression is desired a polyethylene

tube is threaded over the needle prior to its introduction. The needle is then withdrawn at the end of the procedure and the polyethylene tube left in to allow bile drainage.

Indications—The main indications for percutaneous cholangiography are:

1) To rule out hepatocellular disease as the cause of jaundice before surgical exploration. If the examination fails to show an obstruction the operation is cancelled and the patient watched carefully for signs of bleeding or bile peritonitis.

2) To give a visual picture of the location, nature and extent of the pathological process and thereby facilitate and expedite the surgeon's task at operation.

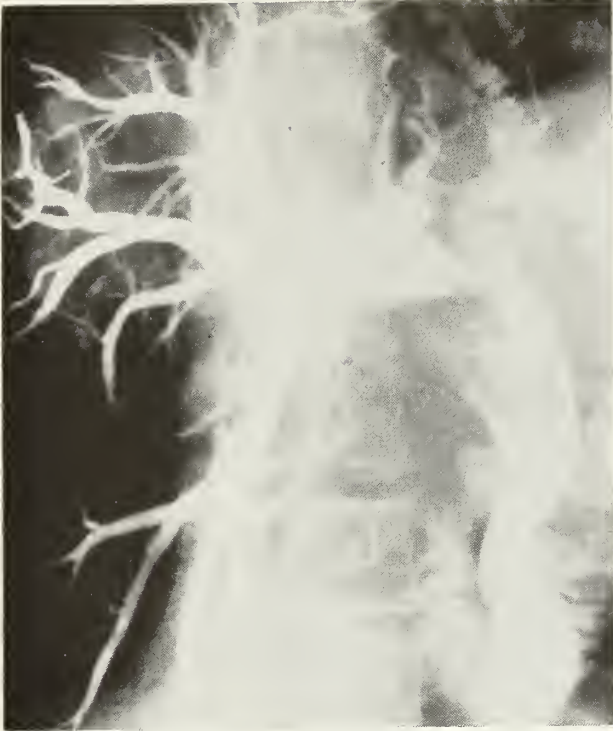
3) To elucidate the status of the biliary tree in cases of biliary atresia.

Radiographic Findings

Calculous disease of the biliary system can be recognized by the demonstration of faceted calculi or a meniscus sign at the site of the obstructing calculus (Fig. 1). Stenosis due to a previous surgical injury or a localized stenosing cholangitis gives a circumferentially narrowed segment with a smooth margin. The segment is usually short in surgical injuries (Fig. 2) and may be of various lengths in sclerosing cholangitis (Fig. 3). No ductal displacement is seen. Malignant conditions of the ampulla of Vater, bile ducts, pancreas, gall bladder or metastatic disease are usually hard to differentiate as it is difficult to be sure of the origin of the mass after it has extended outside its primary site. Early carcinomas of the bile ducts may be recognized by the rigidity and irregularity of the border of the involved segment.

Carcinoma of the ampulla of Vater in its early stage causes dilatation of the common bile duct as well as a ragged irregular margin at the site of obstruction. A still earlier carcinoma gives a meniscus sign at the distal end of the common bile duct (Fig. 4). In carcinoma of the head of the pancreas the common bile duct is usually cut off at various distances from the distal end depending on the site and extent of the lesion (Fig. 5A). As stated above, with the exception of calculous disease and ductal stricture the differentiations between various malignancies of the right upper quadrant is a tentative one. It is almost impossible when the tumor has extended outside its site of origin and has formed a voluminous mass (Fig. 5B). Indeed in such

Figure 1



A. Large calculus lodged at the junction of the cystic and hepatic duct.



B. Meniscus defect at distal end of common hepatic duct caused by an obstructing calculus. Small calculi are also seen in the right hepatic duct.

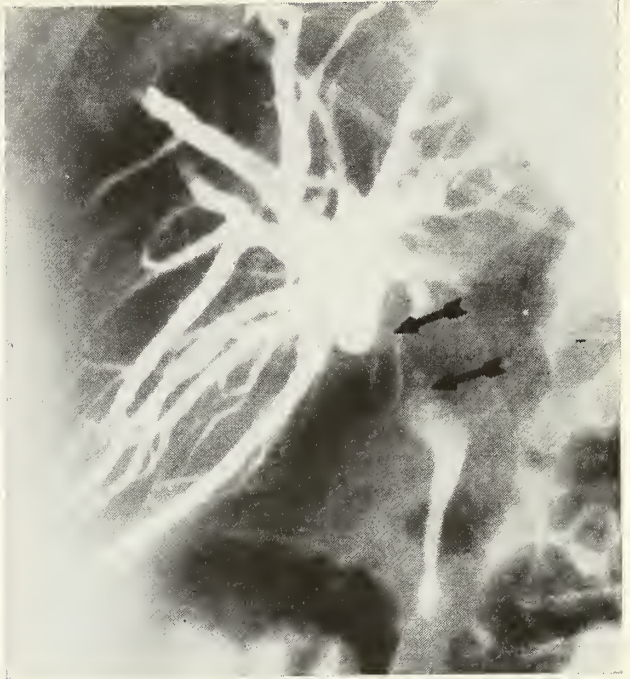


Figure 2

Stricture of the common hepatic duct resulting from a previous exploration and surgical injuries. The localized stenoses is between the two arrows.

cases the surgeon as well as the pathologist have difficulties in diagnosing the site of origin.

Complications—Percutaneous cholangiography is not without hazards. The two main complications are bile leakage leading to bile peritonitis and bleeding due to accidental rupture of a blood vessel. Both of these complications are minimized by the fact that surgery is performed after the examination in the majority of the patients.

In 1966 we reported a series of 140 patients.¹² In this series we had two subphrenic bile collections following cholangiography and the subsequent surgical procedure. Inasmuch as subphrenic collections can occur after operation on the biliary tract, it is hard to determine whether these complications were due to the operation or to the percutaneous cholangiography. Five patients had a mixture of bile and blood in the peritoneal cavity amounting to 500 cc or less, and two patients had 800 cc to 1,000 cc of bile and blood in the peritoneum.

We also had one fatality directly attributable to the procedure. This occurred in a patient with carcinoma of the pancreas and was due to an accidental perforation of a branch of the hepatic artery. Later at operation the bleeding vessel was ligated but the hemorrhage recurred postoperatively and the patient died the following day.



Figure 3

Stenosing cholangitis in a patient with ulcerative colitis and Stevens-Johnson syndrome. Dilated branches of the right hepatic duct are seen. The right hepatic duct is stenosed and only partially filled (arrow). The left hepatic duct and its branches as well as the common hepatic, and common bile ducts are not filled due to extreme stenoses. This information was very helpful to the surgeon in planning his by-pass.



Figure 4

Carcinoma of the ampulla of Vater causing indentation at the distal end of the common bile duct.

Figure 5

When the carcinoma in the right upper quadrant has reached a large size, it is difficult to be sure of its site of origin.



A. Carcinoma of the head of the pancreas.



B. Carcinoma of the common bile duct.



C. Metastases to the porta hepatis from a carcinoma of the stomach.

With the exception of this one fatality all the complications were discovered and easily remedied at operation. In the same publication referred to (12) we made a partial tabulation of patients examined by this procedure in the U.S. and abroad. There were 4 deaths in over 811 patients. The occurrence of fatalities low as they may be is important. However, these must be considered in the light of the anatomic and pathologic information the procedure provides.

Discussion—The question may be asked, why perform a procedure with proven complications when an operation is going to be carried out shortly afterwards, and when the surgeon can inspect the biliary tree and right upper quadrant under direct observation. The answer to this question is that those surgeons familiar with the procedure find that it is rewarding to have a visual anatomic and pathologic picture of the biliary system before exploring the patient. It enables them to plan their anastomoses in the light of the radiographic findings. In cases of obstructive disease of the biliary system any bypass procedure is helpful only if the anastomosed segments are patent. These surgeons also think that the same clear picture may not be easily reached by dissection.

Percutaneous cholangiography will also allow the insertion of a polyethylene catheter for the decompression of the liver and a consequent improvement

of its function prior to the surgical intervention. Improvement of the liver function reduces the surgical morbidity and surgical mortality. Another important benefit that may ensue from percutaneous cholangiography is the occasional demonstration that the biliary tree is patent and the disease is therefore hepatocellular rather than obstructive. This leads to cancellation of the operation. In our previously referred to series of 140 patients¹² five patients were found to have a normal percutaneous cholangiogram (Fig. 6). Their jaundice was cor-

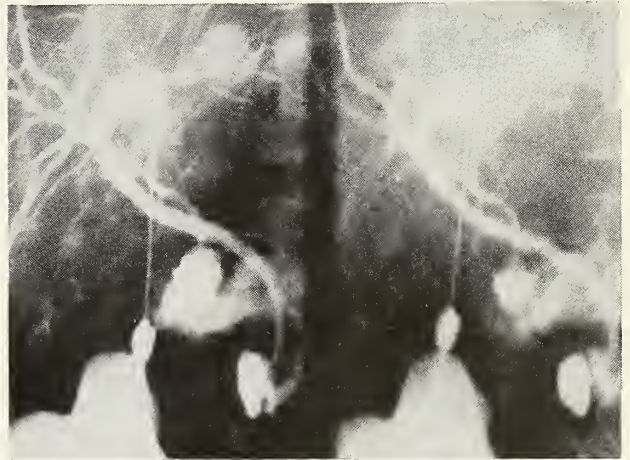


Figure 6

Normal percutaneous cholangiogram. The operation was cancelled and the patient was later discharged with a diagnosis of hepatitis.

rectly diagnosed as non-obstructive and thus an operation was avoided in a high risk group of patients.

Summary

Percutaneous cholangiography is a useful procedure in properly selected patients. It provides a visual picture of the location and extent of the pathological process in patients suffering from obstructive jaundice. It also permits decompression of the liver and thus improvement of its function prior to the surgical procedure. Occasionally this procedure demonstrates that the patient's jaundice is hepatocellular rather than obstructive as diagnosed pre-operatively. The operation is then cancelled to the benefit of the patient. The procedure is not without complications. These, however, must be evaluated in the light of the information sought by the surgeon and its importance to him.

Bibliography

1. Graham, E. A., and Cole, W. H.: Roentgenologic examination of the gall bladder: New method utilizing in-

- travenous injection of tetrabromphenolphthalein. J.A.M.A., 82: 163, 1924.
2. Graham, E. A., Cole, W. H., and Copher, G. H.: Visualizing of the gall bladder by the sodium salt of tetrabromphenolphthalein. J.A.M.A., 82: 177, 1924.
 3. Graham, E. A., Cole, W. H., and Copher, G. H.: Cholecystography: An experimental and clinical study. J.A.M.A., 84: 14, 1925.
 4. Burkhardt, H., and Müller, W.: Versuche über die Perknktion der Gallenblase und ihre Rontgendarstellung. Deutsche Ztschr. f. Chir., 161-162: 168, 1921.
 5. Ifuard, P., and Do-Xuna-Hop: La ponction transhepatique des canaux biliares. Bull. Soc. Med. Chir. Indoch., 15: 1090, 1937.
 6. Royer, M., Solari, A. V., and Lottero-Lanari, R.: La cholangiografia no quirurgica: Nuevo metodo de exploration de las vias biliares. Arch. Argent. de enferm. d. ap. digest. y. de la metricion. 17: 368, 1942.
 7. Carter, F. R., and Saypol, G. M.: Transabdominal cholangiography. J.A.M.A., 148: 253, 1952.
 8. Fuentes, V., Bertoni, C., and Polero, J.: La cholangiografia par puncion hepatica. Prensa Med. Argent., 14: 2873, 1957.
 9. Evans, J. A., Glenn, F., Thorbjarnarson, B., and Mujahed, Z.: Percutaneous transhepatic cholangiography. Radiology, 78: 362, 1962.
 10. Kidd, H. A.: Percutaneous transhepatic cholangiography. Arch. Surg., 72: 262, 1956.
 11. Arner, O., Hagberg, S., and Seldinger, S. I.: Transhepatisk cholangiografi. Nord Med., 65: 730, 1961.
 12. Mujahed, Z., and Evans, J. A.: Percutaneous transhepatic cholangiography. Rad. Clinics N. A. 4: 535, 1966.
 13. Hanafee, W., and Weiner, M.: Transjugular percutaneous cholangiography. Radiology 88: 35, 1967.
 14. Wiechel, K. L.: Percutan transthoracol transhepatisk cholangiografi. Nord. Med., 66: 1029, 1961.

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The Role of Selective Arteriography in the Diagnosis of Gastrointestinal Hemorrhage

Stanley Baum, M.D., Moreye Nusbaum, M.D. and Philip Silverberg, M.D.

Diagnosing the exact site and cause of gastrointestinal hemorrhage remains a problem to all those charged with the responsibility of caring for the bleeding patient. Endoscopic examination, radio-isotope studies and conventional barium examinations fail to demonstrate the site of the bleeding in as many as 20 to 30 percent of cases.^{1, 2} Even when a lesion is demonstrated by these methods, it is uncertain that this is the cause of the patient's hemorrhage. This problem is even further complicated when multiple lesions are shown since any one of them could account for the blood loss, for example, hiatal hernia in a patient with a deformed duodenal bulk.

At exploratory laparotomy the surgeon is unable to find the cause of bleeding in as many as 20 percent of patients operated on for upper gastrointestinal hemorrhage and 70 percent of patients operated on for melena.³

Investigators have attempted to develop more accurate diagnostic methods for the bleeding patient including the fluorescein string test as well as recovery of radio-active isotopes from the gastrointestinal tract after their intravenous injection. Although all of these methods have on occasion been successful, they have not been widely accepted because of their many shortcomings.

Margulis et al in 1960⁴ reported the successful use of operative segmental mesenteric arteriography for the demonstration of a bleeding arteriovenous malformation in the cecum. This method has never become popular as a diagnostic technique because of the many technical difficulties associated with segmental arteriography at the time of laparotomy.

In 1963, Baum et al reported the demonstration of artificially constructed bleeding points in dogs by means of percutaneous selective mesenteric

arteriography.⁵ Because of the ability of the technique to demonstrate bleeding rates as small as 0.5 cc per/min., this technique was utilized clinically in selective patients. The initial experience was reported in 1965⁶ and subsequently re-evaluated in 1967⁷ and 1969.⁸ Since then other investigators have successfully utilized this method.⁹⁻¹³

Specific Sites of Gastrointestinal Hemorrhage Esophagus

Bleeding esophageal varices or a Mallory-Weiss tear represent the most common causes of esophageal hemorrhage. These lesions require specific therapy and it is important for the surgeon to preoperatively establish the correct diagnosis. (Figure 1)

The bleeding patient who has portal hypertension and esophageal varices presents a difficult problem in management chiefly because of the high incidence of bleeding from sites other than the esophagus. These patients will frequently have associated hemorrhagic gastritis and peptic ulcer disease. In such cases, selective angiography is not only of value in demonstrating the varices themselves but also in excluding sources of arterial or capillary bleeding.

More recently attempts have been made to temporarily control portal hypertension and bleeding varices by the selective infusion of vasopressin directly into the superior mesenteric artery.^{14, 15} This infusion has been continued for 3 to 5 days. Because of the reduction in superior mesenteric arterial flow the portal venous return is decreased resulting in up to 50% reduction in the portal pressure. This technique promises to be of great help in the emergency control of patients with bleeding esophageal varices.

Stomach

Bleeding gastric ulcers of various etiologies have been demonstrated by means of arteriography.

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These have included ordinary peptic ulcers, malignant ulcers as well as those associated with severe debilitating diseases, the so-called stress ulcers (Figure 2).

Duodenum

Because of the dual nature of the duodenal arterial blood supply, it is frequently necessary to visualize both the celiac axis and superior mesenteric artery in order to demonstrate the site of duodenal bleeding. Bleeding duodenal ulcers can be readily seen during angiography whether the crater is in the cap or duodenal loop. (Figs. 3, 4 and 5)

Small Intestines

Vascular malformations or the so-called angiodysplasias are much more common than were previously suspected.¹⁶ These patients frequently present with repeated episodes of bleeding, negative barium studies and in many cases negative exploratory laparotomies. It is important to emphasize that malformations of this sort will frequently present no gross abnormality to the surgeon even when his attention is directed to a specific segment of the small bowel by the preoperative arteriogram. This makes the precise preoperative localization of the arterial malformation exceedingly important. (Figure 6)

The angiographic demonstration of bleeding small bowel tumors such as leiomyomas and metastatic neoplasms have been described.

Large Intestines

A bleeding lesion in the large bowel is extremely difficult for the surgeon to detect especially since this organ is partially retroperitoneal and cannot be mobilized as readily as the small intestines. Arteriography is of greatest value in the demonstration of bleeding from those lesions which cannot be visualized by conventional barium studies and are difficult for the surgeon to recognize, such as arteriovenous malformations (Figure 7). Diverticulosis, diverticulitis and other inflammatory lesions may be demonstrated by barium studies, however, the radiographic demonstration of actual bleeding depends on arteriography.

Intra-abdominal Hemorrhage

Intra-abdominal, extraluminal bleeding has been successfully demonstrated by means of arteriography. This includes cases of ruptured splenic artery aneurysms, hepatic artery aneurysms as well

as erosions into major intra-abdominal arterial branches. (Figure 8)

Discussion

The patient who is most likely to benefit from arteriography is the one who has a history of repeated episodes of gastrointestinal bleeding in whom no cause can be demonstrated by means of conventional barium studies. These patients will also frequently have histories of negative exploratory laparotomies. The history is probably the most important factor in determining that group of patients who should have arteriography as the initial diagnostic procedure. If the clinical story fails to suggest the probable cause for the hemorrhage or if the history is confusing and compatible with several possible causes, arteriography might then be considered as the first study. If barium examination is done first, the arteriogram must be delayed until the gastrointestinal tract is cleared of barium. During this delay, the bleeding may stop and the arteriographic demonstration of extravasated contrast material will be impossible.

One of the problems in establishing priorities in the selection of various diagnostic procedures depends on the relative skill with which each can be performed in a given institution. The radiology department that performs very few arteriograms should probably not undertake the performance of emergency arteriography of this type when the patients are acutely ill. Many of the patients referred for these studies are in shock as a result of blood loss and the examination must be performed as rapidly and efficiently as possible. This requires the active participation of both medical and surgical personnel experienced in emergency treatment. The success and safety of the study will obviously depend on the skill of such a team.

Summary

Selective celiac, superior and inferior mesenteric arteriography is an important method for the localization of gastrointestinal hemorrhage. The demonstration of extravasation of contrast material into the gut can be shown only when the patient is actively bleeding, although presumptive sites of hemorrhage have been demonstrated after the patient has stopped bleeding, thus providing useful information. These examinations are frequently performed as emergency studies on critically ill patients. This requires complete familiarity with the technique by thoroughly trained personnel.

Figure 1

Mallory-Weiss tear

A selective celiac arteriogram was performed on this 45-year old man who was admitted to the hospital with massive hematemesis. Because the patient had an alcoholic history, the admitting diagnosis was bleeding esophageal varices.



(A) Selective celiac arteriography during the early arterial phase demonstrates a normal configuration of the celiac axis without any evidence of an arterial malformation.



(B) A film made several seconds after the injection of contrast material demonstrates early extravascular contrast material accumulating high in the fundus of the stomach (Arrow).



(C) During the early venous phase of the examination there is persistence of contrast material high in the cardia of the stomach (Arrows) that is now beginning to exhibit a curvilinear configuration.



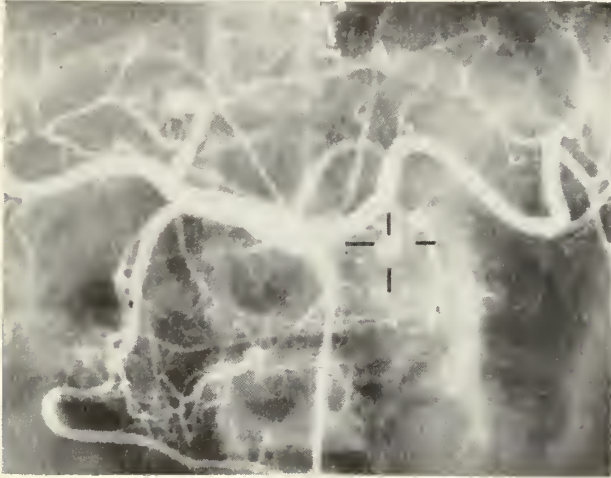
(D) Approximately 28 to 30 seconds after the injection persistence of extravasated contrast material is seen (Arrows) high in the cardia of the stomach.

The venous phase of the study demonstrated normal splenic and portal veins without any evidence of esophageal varices. On the basis of the arteriogram the bleeding was shown to be arterial and originating from the region of the cardio-esophageal junction. The patient was operated on immediately after the arteriogram and a tear in the mucosa of the cardio-esophageal junction was found. This area was oversewn and the bleeding was controlled. The patient had an uneventful postoperative course.

Figure 2

Bleeding gastric ulcer.

This 15-year-old girl had multiple episodes of gastrointestinal hemorrhage that on previous arteriography was shown to be due to arteriovenous malformations of the small intestines. (See Figure 6) Two weeks following the last operative procedure, the patient was studied by means of selective celiac arteriography because of massive hematemesis.



(A) A film in the late arterial phase demonstrates a small amount of contrast material extravasating from a branch of the short gastric artery into the midportion of the body of the stomach (Arrows).



(B) During the late arterial phase of the study, there is an increase in the amount of extravascular contrast material in the body of the stomach (Arrow). Surgical explanation demonstrated a gastric ulcer that was actively bleeding.

Figure 3

Bleeding duodenal ulcer.

This 50-year old woman was hospitalized because of massive hematemesis. There was no prior history of peptic ulcer disease and for this reason an arteriogram was performed as the initial examination.



(A) Selective celiac arteriography demonstrates a small amount of extravasated contrast material extending from a branch of the superior pancreaticoduodenal artery (Arrows).



(B) Selective superior mesenteric arteriography was performed because of the dual blood supply to the duodenum.

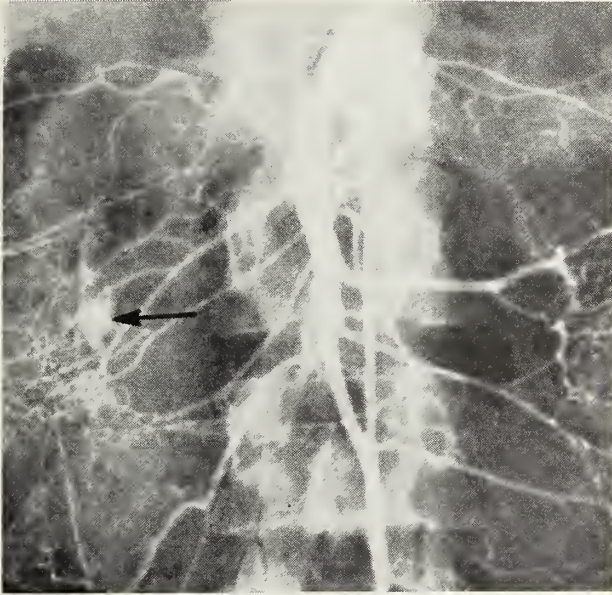


(C) During the late arterial phase of the selective superior mesenteric study, extravasated contrast material is again identified within the duodenal cap (Arrows). Following the arteriogram, the patient stopped bleeding and did well on medical management. A barium examination performed a day after the arteriogram confirmed the presence of a large ulcer in the duodenal cap.

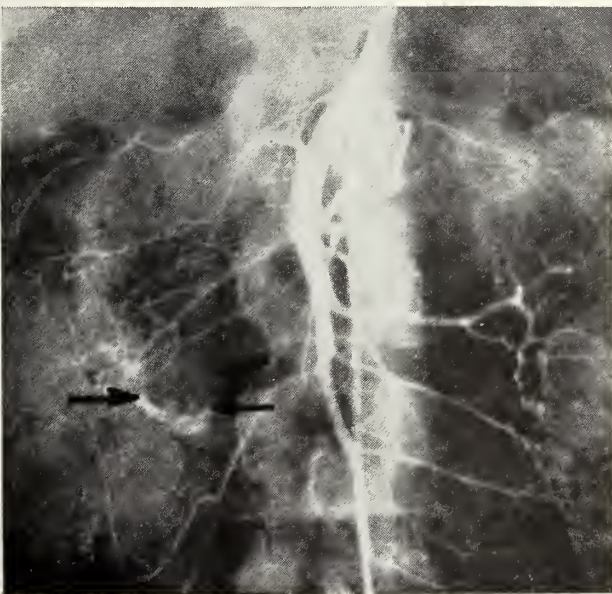
Figure 4

Bleeding ulcer in the duodenal loop.

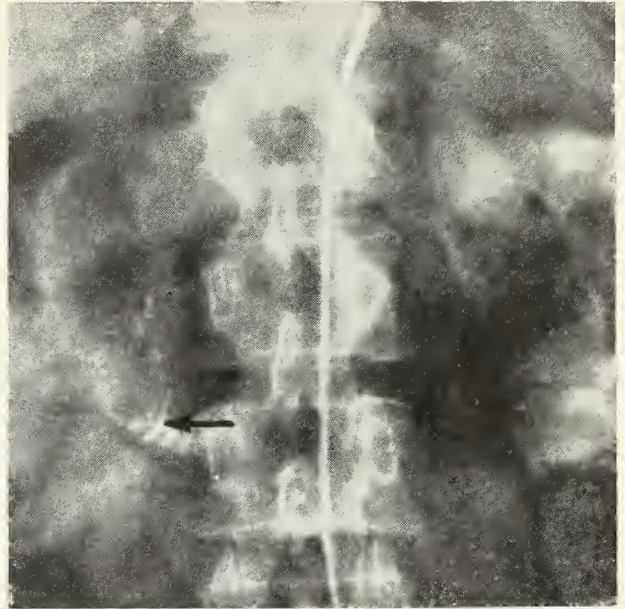
Gastrointestinal bleeding occurred 10 days following aortic valve replacement in a 50-year old man. Emergency arteriography was performed in an attempt to locate the source of hemorrhage.



(A) Immediately following the injection of contrast material into the superior mesenteric artery, extravasated contrast can be identified extending from the branch of the inferior pancreaticoduodenal artery (Arrow).



(B) One and one-half seconds after the injection into the superior mesenteric artery further accumulation of contrast material can be identified within the duodenal loop outlining mucosal folds (Arrows).



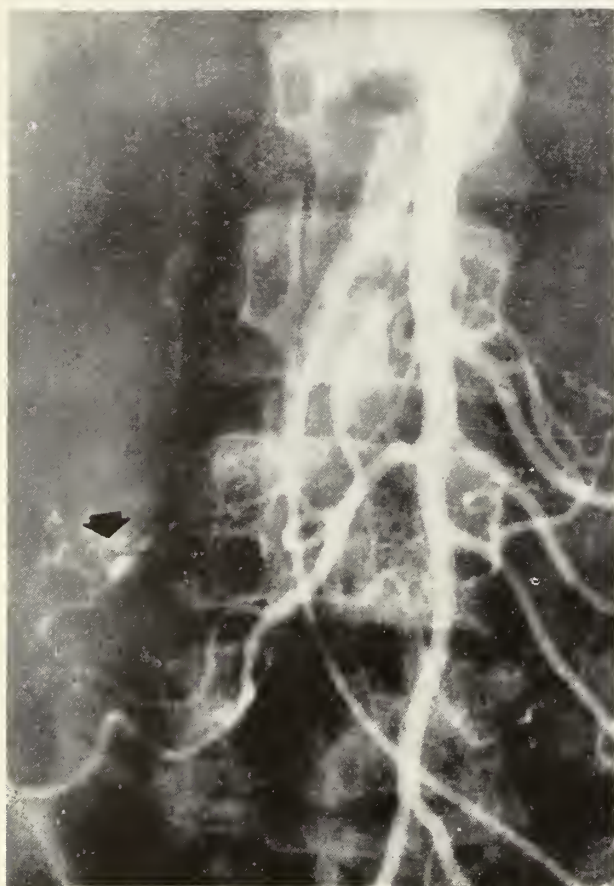
(C) Ten seconds after the injection, contrast material persists within the descending duodenum outlining mucosal folds at the junction of the second and third portions of the duodenum.

Arteriography demonstrated this unusual location for bleeding at the junction of the second and third portion of the duodenum and indicated that the bleeding was arterial in origin. Surgery was performed immediately following the study and the descending limb of the duodenum was opened and a stress ulcer found at the junction of the second and third portions of the duodenum confirming the arteriographic diagnosis. The ulcer was oversewn and the patient had an uneventful postoperative course.

Figure 5

Bleeding Duodenal Ulcer

This 70-year old man with chronic renal failure and azotemia began hemorrhaging from the gastrointestinal tract. Emergency arteriography was performed.



(A) The early arterial phase of the superior mesenteric arteriogram demonstrates a small amount of extravascular contrast material arising from the inferior pancreaticoduodenal artery (Arrow).



(B) Twenty-six seconds after the injection there was persistence of intraluminal extravascular contrast material outlining mucosal folds in the small intestines. A discrete oval collection of contrast suggested an ulcer crater (Arrow).

On the basis of this examination, the site of bleeding was determined to be in the descending duodenum. This was confirmed at surgery.

Figure 6

Arterial-venous malformations

This 15-year old girl had repeated episodes of gastrointestinal hemorrhage. Conventional barium studies of the stomach, duodenum and small bowel were negative and an exploratory laparotomy during a period of hemorrhage failed to disclose the site of bleeding.



(A) Selective superior mesenteric arteriography shows dilatation of the arterial branches supplying the proximal jejunum and there is a rich capillary blush of these loops.



(B) During the early venous phase, there is an intense blush of this portion of the jejunum with very early venous return.

This patient was operated on and the involved segment of jejunum resected. On pathologic section dilated arteries and veins were noted consistent with an arteriovenous malformation. Five months later, however, the patient again experienced acute gastrointestinal hemorrhage and a repeat superior mesenteric arteriogram demonstrated that the distal ileal loops were involved with the same degree of arteriovenous shunting and dilatation as was present previously in the proximal jejunal loops. This case represented an instance of rapidly developing arteriovenous malformations that involved several areas in the small intestines with normal segments of bowel between them.

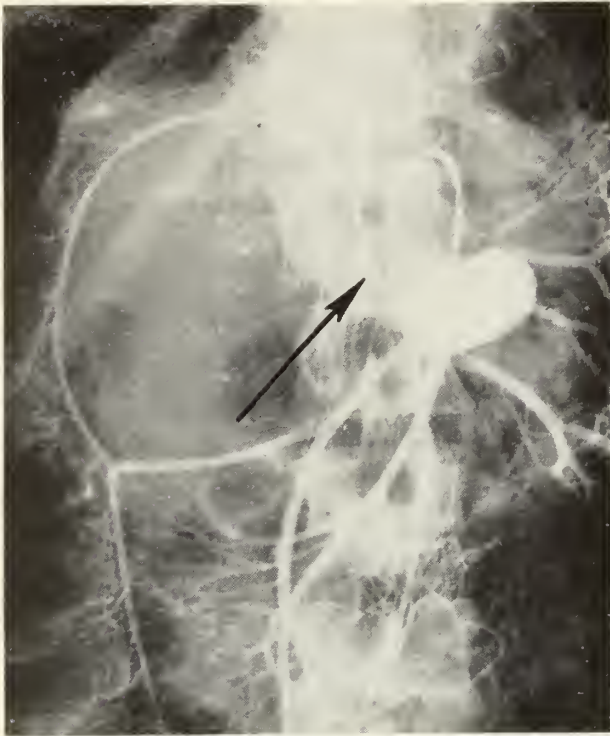
Figure 7

Arteriovenous malformation of the cecum



This 45-year old woman was admitted to the hospital because of massive melena. During the arterial phase of a selective superior mesenteric arteriogram, a large cecal artery could be seen feeding a round vascular lake along the left aspect of the cecal colic junction (Curved arrow). A prominent early draining vein (Straight arrow) is present indicative of an arteriovenous malformation. No other malformation could be identified in either small or large bowel.

Figure 8
Intra-abdominal bleeding due to erosion into the
middle colic artery



This 28-year old man had multiple stab wounds of the abdomen. Following the last episode the patient developed a draining sinus in the left upper quadrant and a small catheter was inserted into this for drainage. One week following the insertion of the drain, the patient began to bleed massively through the abdominal wound. Emergency superior mesenteric arteriography demonstrated massive extravasation extending from a branch of the middle colic artery (Arrow). The patient was operated on immediately following the arteriogram and the middle colic artery was ligated and the bleeding controlled. The patient had an abscess surrounding the previously inserted drain which had eroded into the adjacent middle colic artery.

Bibliography

1. Atik, M., and Simeone, F. A.: Massive gastrointestinal bleeding. *Arch., Surg.*, 69:355, 1954.

2. Cooley, R. N.: The diagnostic accuracy of upper gastrointestinal radiological studies. *Amer. J. Med. Sc.*, 242:628, 1961.
3. Retzlaff, J. A., Hagedorn, A. B., and Bartholomew, L. G.: Abdominal exploration for gastrointestinal bleeding of obscure origin. *J.A.M.A.*, 177:104, 1961.
4. Margulis, A. R., Heinbecker, P., and Bernard, H. R.: Operative mesenteric arteriography in the search for the site of bleeding in unexplained gastrointestinal hemorrhage: A preliminary report. *Surgery*, 48: 534-539, 1960.
5. Nusbaum, M., and Baum, S.: Radiographic demonstration of unknown sites of gastrointestinal bleeding. *Surg. Forum*, 14:374, 1963.
6. Baum, S., Nusbaum, M., Blakemore, W. S., and Finkelstein, A. K.: The preoperative radiographic demonstration of intra-abdominal bleeding from undetermined sites by percutaneous selective celiac and superior mesenteric arteriography. *Surgery*, 58:797-805, 1965.
7. Baum, S., Nusbaum, M., Clearfield, H. R., Kuroda, K., and Tumen, H. J.: Angiography in the diagnosis of gastrointestinal bleeding. *Arch. Int. Med.*, 119:16-24, 1967.
8. Baum, S., Stein, G. N., Nusbaum, M., Chait, A.: Selective arteriography in the diagnosis of hemorrhage in the gastrointestinal tract. *Radiologic Clinics of North America*, 7:131-145, 1969.
9. Annes, G., Caplan, J. H., and Heinlich, H.: Upper gastrointestinal hemorrhage: Undetected site localized by selective arteriography. *Arch. Surg.*, 94:44-45, 1964.
10. Boijesen, E., and Reuter, S. R.: Angiography in the diagnosis of chronic unexplained melena. *Radiology*, 89:413-419, 1967.
11. Kanter, I. E., Schwartz, A. J., and Fleming, R. J.: Localization of bleeding point in chronic and acute gastrointestinal hemorrhage by means of selective visceral arteriography. *Amer. J. Roentgenol.*, 103:386-398, 1968.
12. Kochler, R. P., and Salmon, R. B.: Angiographic localization of unknown acute gastrointestinal bleeding sites. *Radiology*, 89: 244-249, 1967.
13. Reuter, S. R., Bookstein, J. J.: Angiographic localization of gastrointestinal bleeding. *Gastroenterology*, 54:876-883, 1968.
14. Nusbaum, M., Baum, S., Sakiyalak, P., and Blakemore, W. S.: Pharmacologic control of portal hypertension. *Surgery*, 62:299-310, 1967.
15. Nusbaum, M., Baum, S., Kuroda, K., and Blakemore, W. S.: Control of portal hypertension by selective mesenteric arterial drug infusion. *Archives of Surgery*, 97:1005-1013, 1968.

Advances in The Radiologic Diagnosis of Diseases of The Kidney and Urinary Tract

Alan J. Davidson, M.D.

Precision in the diagnosis of disease of the kidneys and urinary tract has been greatly enhanced during the past decade through advances in the field of diagnostic radiology. Greater understanding of the physiologic basis of the intravenous pyelogram, for example, has led to modification of this long accepted procedure to allow a far greater yield of information than could be derived from traditional approaches to this examination. Likewise, innovations and advances in equipment design and capability have allowed the diagnostic radiologist to collect and analyze clinical data in terms of function and with greater precision than has been possible in previous years when description of static morphology characterized the field. Finally, the introduction of new diagnostic methods, particularly those relating to the study of organ vascularity, has expanded greatly the understanding of many abnormalities of the kidneys, improved the accuracy of pre-operative diagnosis, and has placed a new responsibility on the radiologist. The following sections discuss and illustrate in detail many of these advances.

Advances in Intravenous Pyelography

Prior to 1955, agents used to achieve radiopacity following intravenous injection were characterized by moderate capabilities for radiopacity and significant toxicity. Since 1955 a number of agents, all triiodinated benzoic acid derivatives, have been introduced and gained general usage. These agents carry more iodine atoms per molecule and have far less incidence of systemic or specific organ toxicity than those previously available. Based on the realization that these agents have low toxic properties, there has been in the past five years, an increasingly vigorous use of larger doses of these agents for enhancing the quality of the intravenous pyelogram. High dose urography, therefore, has evolved from the introduction of compounds containing larger

numbers of iodine atoms than previously used and has evolved with the knowledge that these agents in larger volumes do not significantly add to the hazards of the intravenous pyelogram.

In addition, there recently has been considerable advance in the understanding of the physiology of excretion of these agents. Accumulated evidence from a number of sources makes it clear that these agents are excreted essentially by glomerular filtration and that they exhibit a strong osmotic diuretic response.^{1, 2} Large volumes of contrast media have been demonstrated to result in a linear increase in the plasma concentration of these agents. Since the quality of the IVP is dependent upon the number of iodine bearing molecules which can be filtered through the glomerulus in a fluid medium sufficient to distend the collecting systems of the ureters and pelvis, these large doses of contrast media increase the filtered fraction of contrast media and, because of these osmotic diuretic actions, achieve a greater distention of the collecting structures of the kidney and ureter. These facts form the basis for the advances which have occurred in the clinical use of intravenous pyelography, specifically in the presence of renal failure and in the delineation of the entire collecting structures of the kidneys and ureter without resorting to retrograde instrumentation.

In the case of renal failure, the clinician must define first of all whether the failure is based on obstruction to urinary outflow or is a reflection of a primary parenchymal process in the kidney. Secondly, if the pathologic process is primarily parenchymal and non-obstructive, the classification of the disease, particularly regarding its duration, is greatly facilitated by the delineation of renal size; large kidneys usually represent an acute process and small ones a chronic process. In 1963, Schwartz *et al*³ pointed out the possibility of achieving diagnostic information from intravenous administration of urographic contrast material in the presence of renal failure. These workers, utilizing relatively small increments above the standard dose, demonstrated their ability to acquire this information in patients whose serum creatinines varied from 2mg% to 10mg%. This study gave impetus to the

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investigation of increasingly higher volumes of contrast material administered to patients in renal failure. Subsequently, there evolved a method of intravenous pyelography which has become known as the drip infusion pyelogram.¹ This procedure has as its basis the administration of contrast material in a dose schedule of 1cc. per pound. While no upper limit of dosage has been established clearly, convention at this time usually limits the total dosage of contrast media to between 150 and 180cc. It has become popular to dilute this contrast material in an equal volume of normal saline or dextrose administered as a rapid intravenous infusion. The essence of the procedure is based, however, on the total dose of contrast material administered. The use of an equal volume of diluent in the drip infusion method is not essential to the success of the method. High dose urography coupled with painstaking attention to technical detail, particularly the use of laminography of the kidneys, has achieved useful information in many patients with profound renal failure. Figure 1, illustrates such a use in a



Figure 1

Successful opacification of the renal parenchyma and faint delineation of a non-dilated pelvocalyceal system in a patient with profound renal failure due to multiple myeloma. A dose schedule of 1 cc. of contrast per pound of body weight was utilized to obtain these results.

patient with a serum creatinine of 28mg%, oliguria, and "large kidney" renal failure due to malignant plasma cell infiltrative lesions of the kidney parenchyma. Not only are the kidneys opacified well enough to determine their size, but the identification of a faint but definite non-distended pelvic and calyceal system allows the diagnosis of a primary parenchymal process rather than urinary tract obstruction. The need for retrograde instrumentation of severely ill patients such as in this case is thereby obviated by the use of this method.

Based on the fact that contrast medium also acts as strong osmotic diuretic agents, it has become apparent that all of the collecting structures of the urinary tract, including the bladder and ureters can become well distended in their entirety and thus subject to accurate radiographic diagnosis following high dose administration of contrast media. This situation is illustrated in figure 2, in which two films obtained on separate days on the same patient, both taken 10 minutes after administration of contrast media are illustrated. In figure 2a, the film was exposed following the administration of the standard dose of opaque material; in figure 2b, the same conditions existed except that a high dose of contrast material was given. It can be seen that in the latter situation, both ureters and the collecting systems are well distended in their entirety whereas they were not on the standard dose examination. The utilization of this method has had the clear-cut result of causing a marked decrease in the frequency with which urologists have to resort to retrograde instrumentation and opacification of the urinary tract for urologic diagnosis. The success

Figure 2

Comparison of degree of distention of pelvocalyceal system and ureters with standard dose urography and high dose urography.



Figure 2a

Illustrates a film taken 10 minutes after administration of a standard dose of contrast media.



Figure 2b

Illustrates the identical conditions but a high dose of contrast material administered. Note the excellent distention of the collecting structures and ureters due to the diuresis produced by the extra amount of contrast media.

of this approach to pyelography is clear from reports from many medical centers where the number of retrograde pyelograms performed annually has decreased markedly in the past five years. Certainly, it is accepted practice now to attempt this type of distention and opacification of the collecting structures through the use of high dose urography prior to subjecting the patient to retrograde instrumentation.

Advances due to Improved and New Equipment

A number of technical advances have occurred over the past decade which have resulted in a marked improvement in the accuracy of radiologic diagnosis of diseases of the kidneys and urinary tract. While the introduction of many of these techniques occurred prior to the present decade, their general application and advanced state of development have characterized more recent times.

Tomography, based on the application of certain geometrical circumstances which exist when the x-ray tube and the film are in certain related motion during the exposure, allows for the production of

films exposed so that structures at specific, determinable levels of the body are focused upon. When tomographic cuts at the level of the kidneys are obtained following the introduction of intravenous contrast material precise definition of the renal structures without overlying spurious shadows is obtained. In this manner, certain abnormalities of morphology of the kidney become manifest particularly in the case of the patient who is poorly prepared or who is unable to attain the usual opacification of the kidney because of functional abnormalities.

The usefulness of this technique has been greatest in the evaluation of mass lesions of the kidneys, particularly in the distinction of solid tumors and benign simple cysts. The ability to distinguish these two categories of mass lesions is based on several factors. First, the simple fluid-containing benign cysts of the kidney, being composed of non-vascularized material, fails to accumulate contrast media within its substance. This in turn results in an area of relative radiolucency on the intravenous pyelogram, most dramatically demonstrated on the nephrotomogram. Furthermore, tomographic cuts of the kidney following the IVP characteristically reveal that the benign cyst is smoothly margined, expands circumferentially in an orderly fashion, and that it tends to have 'claws' or normal staining tissue surrounding it at the lateral margins of the kidney. Contrariwise, the renal solid tumor usually bears a vascular bed which produces radiopacity in the area of the mass lesion, although this area of radiopacity may be mottled and irregular because of incomplete perfusion or necrosis in the tumor. Secondly the solid tumor expands irregularly, invades the adjacent normal tissues so that the margins of the mass are irregular, and does not have a sharply circumscribed interface between the abnormal area and adjacent normal tissue. While these features can often be distinguished on the standard IVP, the nephrotomogram is by far the superior method for demonstrating these changes in the majority of patients; its increasing popular usage has greatly enhanced the information which is obtainable from the IVP. Finally, nephrotomography is useful in determining renal size, the presence of calcifications, and questionable abnormalities of renal contour.

Image intensification, based on the electronic acceleration of the fluoroscopic image is another area of advance which has resulted in greater versatility in the radiologic approach to diseases of the urinary tract. This has been particularly so in regard

to study of the dynamics of the lower urinary tract. Video tape and cine recording of radiographic images, made feasible by image intensification have resulted in considerably improved understanding of problems relating to bladder neck obstruction, vesico-ureteral reflux and ureteral function. While cine recordings of the lower urinary tract, particularly in youngsters, is now considered to result in excessive radiation, other forms of image storage are of equal value and do not have the same radiation hazard. This is true particularly regarding video tape. Certainly the advances in radiologic techniques in this area have made it mandatory to undertake a dynamic study of the lower urinary tract in all patients with recurrent urinary tract infection, particularly in the young and the female patient.

Advances in Techniques

*Cyst Puncture*⁵ Considerable interest has developed in recent years regarding the method of percutaneous puncture of renal mass lesions. Visualization of the kidney is achieved by the intravenous injection of contrast media with localization of the pathologic area by image intensification. With the patient prone, the spinal needle is introduced under television control into the area in question. Once the needle is in place, as determined by fluoroscopy, a number of steps are undertaken. First, partial evacuation of any fluid is performed permitting a cytological evaluation of the fluid; lipid stain is usually performed on the fluid since the presence of fat in the fluid has a significant correlation with the presence of malignancy. Secondly, radiopaque contrast media is injected into the partially evacuated cyst and horizontal beam films taken in multiple projections are obtained so that a double contrast study of the walls of the cyst is available for evaluation. If the wall is smooth, than the reliability of a diagnosis of benign simple cyst is considered to be substantial. On the other hand, blood-tinged fluid removed from the cystic area or the presence of irregularities of the wall of the cyst are strong indications for the presence of a tumor with necrosis. (Figures 3a, 3b and 3c)

The problem of tumor implantation along needle tracts is one which always requires consideration in these circumstances. Substantial clinical

Figure 3

A simple cyst of the lower pole of the left kidney has been percutaneously punctured through the back. Partial evacuation of the fluid has allowed introduction of contrast media and air.



Figures 3a and 3b

Illustrate horizontal beam films obtained with the patient in both decubitus projections.



Figure 3c

Represents the patient in an upright position. These films allow a double contrast examination of the interior lining of the cyst wall. The presence of a smooth margin throughout the cyst indicates a benign simple cyst.

experience with percutaneous biopsies of malignant lesions in other viscera, namely the lung and liver, testify to the overall safety of this type of diagnostic procedure. Usually cyst puncture follows renal arteriography and under these circumstances, the other potential hazard in cyst puncture is circumvented, namely, the introduction of a relatively large bore needle into a vascular structure.

In the differential diagnosis of benign and malignant mass lesions of the kidney, cyst puncture has its greatest advantage in the high risk patient in whom because of age or other infirmities an angiographic procedure or direct operative intervention under anesthesia would represent a risk greater than that related to cyst puncture. Certainly cyst puncture should be strongly considered in this group of patients since the demonstration of changes characteristic of benignancy should militate against surgical intervention.

Renal and Adrenal Angiography. A considerable amount of experience has been accumulated regarding the angiographic diagnosis of diseases of the urinary tract, principally as applied to the kidney.⁶ The application of aortography and selective renal and adrenal arteriography has proven to be particularly useful regarding the diagnosis of mass lesions

in the kidney and retroperitoneum. More recently, selective catheterization of adrenal veins has been introduced⁷ and has greatly enhanced the precision of detecting adrenal pathology while at the same time permitting collection of blood samples from the adrenal gland for chemical determinations. Furthermore, the *in vivo* studies of the renal vascular bed has been of great importance in the understanding of the complex problem of renovascular hypertension.

The plain film of the abdomen, intravenous pyelogram and nephrotomogram serve only to identify the presence of a mass lesion in the kidney. In selected cases, as discussed in the previous section, the percutaneous puncture of mass lesions might further aid in establishing the nature of the pathologic process, particularly in simple benign cysts. Renal arteriography provides a far more substantial opportunity to refine the differential diagnosis of the mass lesion and should be considered a routine procedure in the evaluation of mass lesions of the kidney and retroperitoneum. Most malignant mass



Figure 4

Arterial phase, selective right renal arteriogram illustrates the characteristic neovascularity associated with renal cell carcinoma. There is early opacification of the renal vein indicating numerous arteriovenous shunts.

lesions of the kidney are not only vascularized, but also have a characteristic abnormal appearance to the vascular bed of the tumor. Marked tortuosity and irregularity of the vessels as well as numerous arteriovenous shunts characterize the malignant tumor. (Fig. 4)

In situations in which the characteristic neovascularity of malignancy is not clearly apparent, pharmacologic adjuncts to renal arteriography can be employed, as originally described by Abrams.⁸ This involves the introduction of a small amount of epinephrine through the renal artery catheter followed by a selective renal arteriogram. The tumor vessels of a malignant process characteristically fail to contract following the introduction of epinephrine while normal vessels or non-malignant tumor vessels tend to respond to epinephrine by marked vasospasm. Contrariwise, mass lesions of the kidney reflecting benign tumors tend to have either a diminished or absent vascular pattern or tumor vessels which respond to epinephrine as do normal vessels. Mass lesions due to simple benign cysts are completely avascular and demonstrate splaying of normal renal arteries around the cyst. (Fig. 5a, b) There are, of course, a number of individual situations and specific pathologic entities in which the renal arteriogram does not fit into a specific pattern or in which benign processes may mimic malignant ones. Thus, those hamartoma which have a predominant angiomatous component may simulate the appearance of a malignant tumor. On the other hand, papillary tubular adenocarcinomas tend to be avascular and may have an angiographic appearance which could be confused with a non-malignant disease of the kidney. Occasionally too, the vasculature associated with benign processes respond to epinephrine as in the case of malignant vessels.

Accumulated experience has made it quite clear that in the process of evaluating a mass lesion of the kidney that angiography provides essential information which can be obtained by no other method. The diagnosis of a benign process by angiographic means may preclude exploratory surgery. This is particularly of benefit in that patient who is a high operative risk. In the case of malignant disease, not only can the diagnosis be established with considerable certainty preoperatively, but the other kidney can be screened for abnormality and the projected surgical approach be planned with greater accuracy. The ability to demonstrate extension of a malignant process beyond the kidney into the renal vein or vena cava or to distant areas is of

Figures 5a and 5b



Illustrate characteristic arteriographic pattern in simple cyst of the kidney (same case as illustrated in Figure 3). The lesion is avascular and splays vessels around it.



Figure 5b is the nephrographic phase in which the characteristic interface between the cyst and the normal contrast-bearing tissue is illustrated.



Figure 6

Late arterial and capillary phase aortogram illustrating presence of a large tumor in the lower pole of left kidney with distant metastatic disease in the left portion of the sacrum and left pubis. Distant metastasis from renal tumors can often be identified by their characteristic vascular pattern.

particular value to the urologic surgeon. Such circumstance is illustrated in Fig. 6.

While the presence or absence of adrenal abnormality can usually be established best by clinical and chemical means, the angiographic approach to the adrenal gland permits the accumulation of information regarding the specific site of the abnormality, as well as allows for a determination as to whether the process is unilateral, bilateral or involving multiple loci. This has been particularly useful in the diagnosis of pheochromocytoma in which tumor not infrequently occurs at one or more of many sites. With the introduction of selective adrenal venography, precision in the diagnosis of small tumors of the adrenal gland and the distinction between hyperplastic and neoplastic processes of the adrenal gland has been greatly enhanced. Figure 7 is an example of a selective adrenal venogram in a patient in whom a clearcut distinction between adrenal carcinoma and adrenal hyperplasia could not be made with certainty by clinical and chemical means. In this case, the demonstration of an enlarged left adrenal gland with normal intrinsic venous architecture established the diagnosis of adrenal hyperplasia.

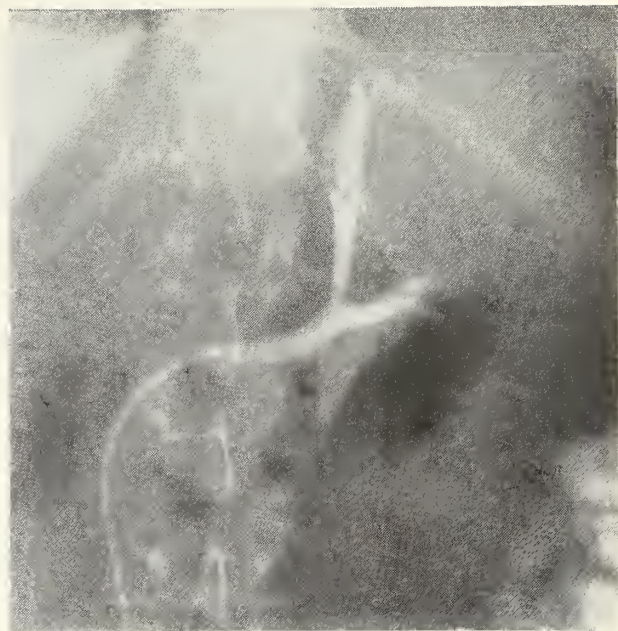


Figure 7

Adrenal venogram performed percutaneously through the right femoral vein. The inferior adrenal vein drains into the left renal vein. The intra-adrenal venous structures are opacified and outline an enlarged left adrenal gland.

Aortography and selective renal arteriography play a basic role in the evaluation of the hypertensive patient for the possibility of renovascular hypertension. While it is well known that the simple presence of a stenotic lesion in the renal vascular bed may not be related etiologically to hypertension, it is essential that renal angiography be performed in those patients in whom clinical or other laboratory tests establish a reasonable suspicion that the hypertension is on a renovascular basis. The application of angiographic techniques to the hypertensive population has revealed that not only the traditional arteriosclerotic lesion of the proximal renal artery may cause renal ischemia but also that a group of other diseases of the renal arterial tree, namely fibromuscular dysplasia, exists and is frequently related to hypertension. In the detection of these lesions, it is important to remember that they frequently exist far distal to the main renal artery and thus can often only be diagnosed by careful selective renal arteriographic techniques. Figure 8 represents such a case in which the lesion was in a segmental interlobar artery.

Summary

Accuracy in the diagnosis of diseases of the kidneys and urinary tract can be achieved by the application of a variety of radiological techniques.



Figure 8

Aortogram in young hypertensive male demonstrating the presence of a segmental interlobar artery dysplastic lesion with post-stenotic dilatation.

These techniques, varying from the simple intravenous pyelogram to more complicated procedures such as opacification of selective vascular structures achieve their greatest usefulness when applied in a logical sequence determined by the particular situation under study. Once so applied, a substantial amount of information can be derived from the radiologic techniques available and a rational therapeutic approach formulated.

Bibliography

1. Cattell, W. R., Fry, I. K., Spencer, A. G. and Purkiss, P. Excretion Urography I: Factors Determining the Excretion of Hypaque. *Brit. J. Radiol.* 40:561-580, 1967.
2. Bemess, G. T., Urographic Excretion Study, Contrast Agents. *Australasian Radiol.* 12:245-251, 1968.
3. Schwartz, W. B., Hurwit, A., and Ettinger, A. Intravenous Urography in the Patient with Renal Insufficiency. *NEJM* 269:277-283, 1963.
4. Schenker, B. Drip Infusion Pyelography: Indications and Applications in Urologic Roentgen Diagnosis. *Radiol.* 83:12-30, 1964.
5. Lang, E. K. The Differential Diagnosis of Renal Cysts and Tumors. *Radiol.* 87: 883-888, 1966.
6. Bookstein, J. J. and Stewart, B. H. The Current Status of Renal Arteriography. *R. Clin. No. Amer.* 2:461-482, 1964.
7. Reuter, S. R., Blair, A. J., Schteingart, D. E. and Bookstein, J. J. Adrenal Venography. *Radiology* 809:805-814, 1967.
8. Abrams, H. L. The Response of Neoplastic Vessels to Epinephrine in Man. *Radiology* 82:217-224, 1964.

The movement of plants toward the light and the search for truth by means of mathematical analysis—aren't these essentially phenomena of the same order? Are not these the last links in the almost endless chain of adaptations made in the whole living world?—I. P. Pavlov.

THE PRESIDENT'S PAGE

Christmas is the traditional season of rejoicing strengthening our faith, our love and our compassion. To many believers this occurs at different times of the year. To most in our country, it is late December. And thus, the timely "Merry Christmas to all." May the New Year bless you with health and happiness.

Our faith is strengthened daily in our prayers and in our actions. A devout believer does not have to read his "bible" all day to express faith. Often his actions may speak louder than his words. Our love for our God, our family and friends, was once expressed by Reverend S. M. Shoemaker, Rector of Calvary Church, Pittsburgh. He emphasized fifteen notable characteristics of love, some of these being that "(1) love is slow to lose patience, (2) love looks for a way of being constructive, (3) it is not possessive, (4) it does not cherish inflated ideas, (5) loves does not pursue selfish advantage, (6) it does not compile statistics of evil, (7) it knows no limit to its endurance, (8) love knows no end to its trust and (9) love can outlast anything." Compassion is an inherent, inescapable characteristic of the true believer. It must be spontaneous, endless and sincere. It cannot make exceptions or partial judgments. Characteristically during the Christmas season, faith, love and compassion "sprouts" in all believers.

This century has witnessed the introduction of Ecumenism on a scale greater than anyone's imagination. Would it be a prophecy or sheer heresy to see an "Ecumenical Christmas" in this country in the not too distant future? Perhaps the closest expression to a true Ecumenical greeting was made by Fra Giovanni—A.D. 1513 when he said:

"I salute you. I am your friend and my love for you goes deep. There is nothing I can give you which you have not got; but there is much, that, while I cannot give it, you can take. No heaven can come to us unless our hearts find rest in today. TAKE HEAVEN- No peace lies in the future which is not hidden in this present little instant. TAKE PEACE! The gloom of the world is but a shadow. Behind it yet within our reach is Joy. There is a radiance and glory in the darkness, could we but see // and to See we have only to Look. I beseech you to look. Life is so generous a giver, but we, judging its gifts by their covering, cast them away as ugly or heavy or hard. Remove the covering and you will find beneath it a living splendour, woven of love, by wisdom, with power. Welcome it, grasp it, and you touch the Angel's hand that brings it to you. Everything we call a trial, a sorrow, or a duty, believe me, that Angel's hand is there; the gift there, and the wonder of an overshadowing Presence. Our joys too: be not content with them as JOYS. They, too, conceal diviner gifts. Life is so full of Meaning and Purpose, so full of Beauty // beneath its covering // that you will find earth but cloaks you heaven. Courage then to claim it: that is all! But courage you have; and the knowledge that we are pilgrims together, wending, through unknown country, home.

And so, at this CHRISTMAS time, I greet you. Not quite as the world sends greetings, but with profound esteem and with the PRAYER that "for you now and forever, the days break, and the shadows flee away."

Again, Merry Christmas to all and best wishes for a healthy and happy New Year.

Stevens J. Martin, M.D.

FROM THE EXECUTIVE DIRECTOR'S OFFICE

WILLIAM R. RICHARDS, M.D. *Executive Director*

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Josephine P. Lindquist
Associate Executive Director

SUMMARY OF ACTIONS

COUNCIL MEETING

Thursday, October 9, 1969

I. Attendance

Present in addition to the Chairman, Dr. S. J. Martin, were: Drs. Graunoff, Brandon, Abbot, Fabro, Harwood, Wilson, Jr., Roch, Nemoitin, Friedberg, Johnson, McDonald, Root, Jr., vonGlahn and Palomba.

Also present were: Mrs. Lindquist, Mr. Douelan (AMA) Dr. Hess (State Welfare Department), Mr. Villano and Dr. Richards.

Absent were: Drs. Weber, Jr. Edson, Dean, Gardner, Polivy, Rogol, Cramer, Farrell, Petrie, Purnell, Grant, Gorin, Pelz and Klare.

II. Routine Business

Approval of Minutes

As printed and distributed, it was VOTED to approve the minutes of the meeting of September 10, 1969, noting one correction; i.e., that the dates for the 1971 Annual Meeting should read "April 27-28-29, 1971" instead of "April 28-29-30, 1971".

Life Membership

It was VOTED to approve applications for Life Membership received from the following Active Members:

Robert W. Butler, Waterbury (NHICMA)—1970
Arthur J. Connolly, New Haven (NHGMA)—1970

Election of Student Members

It was VOTED to elect to Student Membership 23 Connecticut residents who are enrolled in medical schools in the United States and Canada. The names of those elected will be published in the Journal.

Committee Resignations, Appointments, etc.

(a) Subcommittee to Study and Revise the Bylaws:

It was VOTED to accept with regret, and expression of sympathy, the resignation of Nathan H. Friedman, Stratford, as a member of this Subcommittee.

(b) Judicial Committee: It was VOTED to elect Clarence W. Harwood, Middletown, a member-at-large of the Judicial Committee for the term 1969-73, replacing John R. Egan, Old Saybrook, deceased.

Date of Next Meeting

The date for the next Council meeting was set for Wednesday, November 19, 1969.

CRMP

Resolutions from Medical Staffs re CRMP: It was VOTED to receive as information notice from CRMP that the medical staffs of seven Connecticut hospitals had sent resolutions to CRMP urging that there be greater representation of practicing physicians on the CRMP Advisory Board and Executive Committee. Also received as information was notice that the Fairfield Association Board of Trustees had addressed a similar expression of opinion to the Chairman of the CRMP Advisory Board.

Communication from Governor Dempsey

It was VOTED to receive as information a letter from the Governor which was in response to a letter sent to him by the Executive Director, protesting the public charges of several legislators that the medical profession was responsible for the cutbacks in the levels of income and assets regarding eligibility for Medicaid benefits which had been made by the General Assembly. In brief, the Governor expressed agreement with the points of view presented by the Executive Director.

Report—Subcommittee to Study and Revise the Bylaws

The Council received a comprehensive report from this Committee which covered a whole series of Bylaw matters which had been referred to it by the Council during the past 18 months. It was VOTED to approve the report as-a-whole, after making several changes in the wording of several sections.

Progress Report—Ad Hoc Committee on Administrative Organization and Planning

It was VOTED to accept as information a progress report filed by the Ad Hoc Committee on two

matters which had been referred to it by the Council for study. On the two major sections of the report, the Council took actions as follows:

- (a) It was VOTED (7-5, with three abstentions) to approve a recommendation of the Ad Hoc Committee, that, initially at least, a qualified lay person be sought for employment by the Council as Assistant Executive Director. Strong feeling was expressed, however, that if an interested and qualified physician came to the Committee's attention, this action should not preclude his being given consideration.
- (b) It was VOTED to receive as information the Committee's report that the suggestion that the Society consider employing additional specialized staff personnel (an attorney, an actuary, etc.) had been given brief initial consideration, and that it was planned to study this matter further in consultation with Charles Polivy, Hartford, who made the suggestion to the Council originally.

Statement re Medicaid Payments for Physicians' Services in Emergency Rooms

It was VOTED to receive as information a statement on this subject which had been presented by Charles Polivy, Hartford, Chairman of the Liaison Committee with the Welfare Department, to a meeting of the Hospital Cost Commission, 9/29/69. In brief, the statement pointed out the confusion that exists throughout the state as to when a physician may be paid, and when not paid, for services rendered to Medicaid beneficiaries in hospital emergency rooms; made a plea that the hospital service component and the professional service component of charges be clearly defined, no matter what method of billing is used; and the Commission's present policy with respect to such payments to physicians be reviewed with the objective of making it sufficiently flexible to accommodate the various types of arrangements for physician coverage of emergency rooms that are in effect in the various hospitals in the state, and the various rules of the medical staffs that define the limits of treatment that generalists and specialists may perform.

Appointments to Study Committee on Emergency Room Services

In response to a request of Mr. Edward S. Karnasiewicz, Executive Director of the Connecticut Hospital Cost Commission, it was VOTED to request the President to designate four interested and qualified members of the Society to serve on a special committee being formed by Mr. Karnasiewicz

(with four hospital administrators and several members of the Commission) to make a comprehensive study of the problems connected with the rendering of physicians' services to Medicaid beneficiaries in the emergency room setting and payment therefor by the Welfare Department.

Dr. Martin will ask the following CSMS members to serve:

Charles Polivy, Hartford
Charles H. Audet, Jr., Waterbury
Andrew F. Turano, Middletown
Arthur D. Keefe, Hartford

Resolutions to be Transmitted to AMA

A series of six resolutions (Dr. Fabro-5; Dr. Granoff-1) were considered by the Council for introduction by the Connecticut Delegation at the next meeting of the AMA House of Delegates, Denver, Colorado, November 30-December 3, 1969. Of the six resolutions, three were adopted by the Council, as amended. The "Resolves" were:

(1) SUBJECT: COST CONTROL OF HOSPITAL SERVICES

RESOLVED: That the House of Delegates of the American Medical Association express deep concern about the ever-increasing costs of hospital care services; and be it further.

RESOLVED: That the House of Delegates request the Board of Trustees to urge the American Hospital Association and its member hospitals to institute immediately cost control measures designed to stem the tide of rising hospital costs.

(2) SUBJECT: COMPENDIUM OF FEDERAL STATUTES AND REGULATIONS

RESOLVED: That the House of Delegates of the American Medical Association request the proper Congressional agency or the Department of Health, Education and Welfare to publish an annual compendium of the federal laws applicable to health and medicine, with the rules and regulations of administrative bodies which pertain thereto, so that the public, all concerned parties and the medical profession can remain fully and currently informed about legislation in this field.

(3) SUBJECT: MINIMUM WRITTEN PROCEDURES FOR HEARINGS ON HOSPITAL PRIVILEGES

RESOLVED: That the House of Delegates of the American Medical Association express dissatisfaction with the lack of minimal written procedures for hearings on hospital privileges in the "Proposed Standards for Accreditation of Hospitals"; and be it further

RESOLVED: That the House request the AMA Board of Trustees, in consultation with the Legal Department, to draw up and insist on the inclusion of provision for minimal written procedures in any such hearings.

**Nominations to Board of Trustees,
Connecticut Hospital Planning Commission**

It having been reported that two of the six physicians originally nominated by the Council to serve as members of the Board of Trustees of the CHPC are completing their current terms, the Council VOTED to nominate two physicians to fill these posts as members of the CHPC Board. By written ballot, those selected for nomination were:

Bernard A. Burnham, Waterbury
Edward A. Palomba, Somers

Report—Committee on Third Party Payments

A two-part report submitted by the Committee was acted upon as follows:

- (1) It was VOTED to approve a policy statement on third party payments based on fixed payment schedules as follows:
 - (a) The Connecticut State Medical Society recognizes the right of any physician to submit a claim for his usual fee as payment for services provided to Medicaid beneficiaries.
 - (b) The Connecticut State Medical Society expects that the State Welfare Department, administrator of the Medicaid program, will honor its own Medicaid fee schedule.
 - (c) The Connecticut State Medical Society should vigorously oppose any attempt by the State Welfare Department to withhold payment of its fee from the physician until the physician has submitted a claim for payment which reflects the fee set by the department.
 - (d) The State Welfare Department should be urged to pay its claims promptly even

though the amount charged in the submitted claim differs from the established fee.

- (e) These policies shall apply to all third party payors.

It was further VOTED to request the Liaison Committee with the Welfare Department to transmit the foregoing statement of policy to Commissioner Bernard Shapiro.

- (2) It was VOTED to accept the report submitted by the Committee on progress and further plans for updating the Relative Value Schedule, and to approve its recommendations as follows:

- (a) That the Committee be authorized to suspend temporarily its project of updating the 1964 CMA (1965 CSMS) Relative Value Studies; to make a detailed evaluation of the new 1969 CMA Relative Value Studies; and to apply to the 1969 CMA Studies, wherever appropriate, the recommendations for change gathered during the past year from the participating CSMS Sections and allied groups.
- (b) That, for the time being, the present official CSMS Relative Value Schedule be retained as an interim guide in matters having to do with relative values.
- (c) That the Council give approval, in principle, to the 1969 CMA Relative Value Study with respect to the coding and descriptive terminology *only*, and direct the Committee on Third Party Payments to utilize this coding and descriptive terminology in its further efforts to develop a complete, up-to-date RV Schedule for subsequent adoption by the Society.
- (d) That, pending evaluation and report by the Committee on Third Party Payments, the Council take no position on the changed relative value units and other revisions (from 1964) made in the 1969 CMA Relative Value Studies.

Report—Committee on National Legislation

It was VOTED to receive as information, and with thanks, a report submitted by Bernard A. Burnham, Waterbury, Committee chairman, which recounted the experiences and activities of the "Congressional Contact" delegation of Committee members and CSMS officers that visited with Connecticut legislators in Washington, D.C., September

17-18, 1969. It was pointed out by several of the members of the Council who had made the trip that the wording of one section of the report was misleading; i.e., that, in discussing restoration of funds previously cut from the Health Professional Loan Program, Senator Ribicoff's administrative assistant had not really said that "more doctors were not needed at all", but, rather, had made the point that developing newer methods of delivering health care was felt by the Senator to be of equal or greater importance than just increasing the number of physicians *per se*.

Communication: HCMA Board of Directors

It was VOTED to receive as information a communication from the Board of Directors of the Hartford County Medical Association, and, further, to refer the communication to the Committee on Third Party Payments for study and report. In brief, the communication expressed the view of the HCMA Board that the present socio-political-medico-economic picture makes it highly desirable for the Society to develop an insurance or prepayment mechanism (CSMS foundation, partnership with third party payors, etc.) which would provide for 100% payment of physicians' charges and would enable the Society to "act as a third party endorser of the contractual obligations arrived at between labor and management". The development of such a mechanism, in the HCMA Board's opinion, might forestall the further intervention of federal and/or state agencies in the field of third party payment for physicians' services.

Medicaid Non-Developments

The Council made a brief, but comprehensive, review of all developments regarding the Medicaid Program since the termination of the "usual and customary" trial year on March 1, 1969, and since the adjourning of the 1969 General Assembly in June. In summary, it appears that the Society, through representatives, has continued to meet, communicate and cooperate with state agencies and the commissioners thereof that are concerned with establishing a revised Medicaid Program for the biennium, but that said state agencies and commissioners have done very little by way of communicating and cooperating in return. As an example, the Society complied with every request made of it with respect to helping to determine whether a flexible payment schedule (rather than a fixed one) is not possible under the July regulations issued by the Department of HEW, yet nearly four months have elapsed since this study was

initiated and no response whatever has been received from either the Commissioner of Welfare or the Commissioner of Finance and Control. Meanwhile, due to continuing uncertainty and confusion about the program, it is reported that many physicians are "dropping out" of participation in Medicaid.

After considerable discussion, it was VOTED to direct the Executive Director to communicate to Welfare Commissioner Shapiro the Council's deep concern that this protracted delay in departmental decision-making may further jeopardize the efficacy of the Medicaid program, and the Council's strong feeling that it is entitled to a prompt and specific response from the several state agencies involved in return for the cooperation it has given freely to such agencies. A copy of this communication is to be sent to Governor Dempsey for his information. It was further VOTED to apprise the Liaison Committee with the Welfare Department of this action, and to urge the Committee to vigorously pursue the subject matters with Commissioner Shapiro and his staff.

Ad Hoc Committee on Award for Service

Acting on a recommendation of the Fiscal Advisory Committee, the Council VOTED unanimously to appoint an Ad Hoc Committee, composed of the Immediate Past President (Dr. Gardner), the President (Dr. Martin), the President-Elect (Dr. Granoff) and the Executive Director (Dr. Richards), to plan and implement arrangements to give appropriate recognition to the twenty-five years of competent and dedicated service contributed to the Society and its members by Mrs. Josephine P. Lindquist, Associate Executive Director. It was further VOTED to implement the arrangements made by the Ad Hoc Committee at the December semi-annual meeting of the CSMS House of Delegates.

The Connecticut State Medical Society offers placement assistance through the Physicians Placement Service, 160 St. Ronan Street, New Haven, Connecticut, 06511. This service is for the use of physicians seeking locations, as well as physicians seeking associates, and is without charge.

Welcome, New Members

Fairfield County

- Neil Auerbach, M.D., 166 East Avenue, Norwalk, Conn. 06851.
- Andre M. Bersier, M.D., 2660 Main Street, Bridgeport, Conn. 06606.
- David M. Brody, M.D., 10 Mott Avenue, Norwalk, Conn. 06850.
- Sherman M. Bull, M.D., 125 Strawberry Hill Avenue, Stamford, Conn. 06902.
- Robert D. Cottle, M.D., 125 Strawberry Hill Avenue, Stamford, Conn. 06902.
- William G. Covey, M.D., 2875 Main Street, Stratford, Conn. 06497.
- Morton G. Feldman, M.D., 881 Lafayette Street, Bridgeport, Conn. 06603.
- Adolph S. Flemister, M.D., 944 Fairfield Avenue, Bridgeport, Conn. 06605.
- Albin A. Galuszka, M.D., 113 Deer Hill Avenue, Danbury, Conn. 06810.
- Helen L. Griffiths, M.D., 1 Atlantic Street, Stamford, Conn. 06901.
- James T. Kauders, M.D., 2616 Main Street, Bridgeport, Conn. 06606.
- Alan D. Lieberman, M.D., 125 Kings Highway, North, Westport, Conn. 06880.
- Thomas J. Rainville, M.D., 1867 Summer Street, Stamford, Conn. 06905.
- Melville P. Roberts, M.D., 5 Elmerest Terrace, Norwalk, Conn. 06850.
- Harold J. Sherrington, M.D., 8 Weil Street, Stamford, Conn. 06905.
- Arvid C. Sieber, M.D., 120 Long Ridge Road, Stamford, Conn. 06904.
- James K. Spence, M.D., 90 Main Street, Ridgefield, Conn. 06877.
- Richard J. Walsh, M.D., 719 East State Street, Westport, Conn. 06880.
- Alan Weisel, M.D., 47 Oak Street, Stamford, Conn. 06905.
- James W. Wood, M.D., 56 Lafayette Place, Greenwich, Conn. 06830.

Hartford County

- Dorothy K. Brandon, M.D., McCook Hospital, Hartford, Conn. 06112.
- H. David Crombie, Jr., M.D., 85 Jefferson Street, Hartford, Conn. 06103.
- Burton M. Cunin, M.D., 100 Constitution Plaza, Hartford, Conn. 06103.
- Richard A. Dickey, M.D., One Mill Lane, Farmington, Conn. 06032.

- Bennett I. Enowitch, M.D., 60 Washington Street, Hartford, Conn. 06106.
- Stanley P. Filewicz, M.D., 55 West Main Street, New Britain, Conn. 06051.
- Robert Flescher, M.D., 21 Woodland Street, Hartford, Conn. 06105.
- Donald R. Grayson, M.D., 60 Washington Street, Hartford, Conn. 06106.
- David H. Hild, M.D., 85 Jefferson Street, Hartford, Conn. 06103.
- Cyril K. Kim, M.D., McCook Hospital, Hartford, Conn. 06112.
- Morton D. Kurland, M.D., 125 LaSalle Road, West Hartford, Conn. 06107.
- Lester G. Matthews, M.D., 81 South Main Street, West Hartford, Conn. 06107.
- Burton M. Meisner, M.D., 257 East Center Street, Manchester, Conn. 06040.
- Harold Moskowitz, M.D., Mt. Sinai Hospital, Hartford, Conn. 06112.
- Harold R. Nix, M.D., 191 Main Street, Manchester, Conn. 06040.
- Joseph R. Polidoro, M.D., 140 Woodland Street, Hartford, Conn. 06105.
- John T. Price, M.D., 2900 Main Street, Glastonbury, Conn. 06033.
- Leonard M. Selsky, M.D., 683 Farmington Avenue, Bristol, Conn. 06011.

New London County

- Gilbert T. Bergendahl, M.D., 120 Lafayette Street, Norwich, Conn. 06360.
- George Burton, M.D., 488 Montauk Avenue, New London, Conn. 06320.

Litchfield County

- John S. Glenn, M.D., 24 Church Street, Torrington, Conn. 06790.
- Norman E. Smith, Jr., M.D., 71 Spencer Street, Winsted, Conn. 06098.

Middlesex County

- Dominick H. Cerritelli, M.D., 45 Crescent Street, Middletown, Conn. 06457.
- Richard O. Gritzmacher, M.D., 840 Boston Post Road, Old Saybrook, Conn. 06475.
- Martin S. Nadel, M.D., Middlesex Memorial Hospital, Middletown, Conn. 06457.
- Leonard Stoane, M.D., Middlesex Memorial Hospital, Middletown, Conn. 06457.

Placement Opportunities

PHYSICIAN, to cover every other weekend and certain holidays, a well organized general practice consisting mostly of adults, and no one under the age of ten. Salary is \$1300.00 a year plus the fees collected.

HOUSE PHYSICIAN, full time, to cover emergency room and house. Night coverage. Must have Connecticut license. Apartment provided; good fringe benefits. Write P.O. Box 3494, Bridgeport, Connecticut 06605.

ONE YEAR PSYCHIATRIC RESIDENCY at 3rd year level for year beginning July, 1970. AMA approved. Unique opportunity to prepare for private practice and community psychiatry. Supervised intensive, dynamically oriented psychotherapy emphasized. Experience in meaningful application of psychopharmacological agent and somatotherapy. Work with adults and children in residential and outpatient setting. Stipend \$16,500 per annum, with major medical insurance benefits. For information, write Charles P. Neumann, M.D., Medical Director, The Silver Hill Foundation, Box 1177, New Canaan, Connecticut 06840.

CHIEF OF MEDICINE—At accredited State Veterans general medical and surgical hospital of 496 beds, with a domiciliary section of 800 beds. Hartford area. Duties: Directs the facility's program in medicine; related work as required. Age limit: Up to 65 years, if in good health. Experience and training: Completion of general internship in AMA-approved hospital, and not less than 5 years employment with emphasis in the field of medicine and/or certain equivalent qualifications to be evaluated individually. Salary range—Open. For further information and application forms, write to: Frank Mongillo, M.D., Chairman, Veterans Home and Hospital Commission, Rocky Hill, Connecticut.

GENERALISTS, INTERNISTS AND PEDIATRICIANS—Northern Connecticut city of 47,000 in need of 2 General Practitioners, 2 Internists and 1 Pediatrician. Can readily be assimilated into physician community over next 3 years. Hospital privileges available; also good office space available near hospital. Those interested in establishing solo practice in the fields named may obtain further information from: Martin Duke, M.D., Director of Medical Education, Manchester Memorial Hospital, Manchester, Connecticut 06040.

DERMATOLOGIST WANTED — Board certified or eligible, Army requirements fulfilled, for association with New Haven Dermatologist with active and growing practice.

GENERAL PHYSICIAN—with interest in psychiatry. Part-time or contract to cover routine hospital services. Nights and/or weekends. For information write or call Superintendent, Undercliff Mental Health Center, Meriden, Connecticut 06450.

STAFF PSYCHIATRIST—wanted full time or part time to direct therapeutic program in multidisciplinary team. Salary range \$18,520-\$23,755. Complete tax-free maintenance at nominal costs. For information write or call: Superintendent, Undercliff Mental Health Center, Meriden, Connecticut 06450.

PEDIATRICIAN—Needed by small community in eastern Connecticut. Former pediatrician recently withdrew from practice to take fellowship training. Local hospital is well staffed with specialists in various fields. Those interested in obtaining further information about this opportunity may contact: Edmond B. Raheb, M.D., Chief, Department of Obstetrics and Gynecology, Day Kimball Hospital, Putnam, Connecticut.

BOARD INTERNIST — For progressive 300-bed Hebrew Home for Aged, Chronic Disease Hospital License application in process, associated with large general hospital, medical school affiliation possible, salary negotiable. Send C.V. to: Benjamin E. Cohen, Chairman, Medical Conference Committee, The Hebrew Home, 615 Tower Avenue, Hartford Connecticut 06112.

PHYSICIAN who will be willing to work on a salary basis for one or two years with an opportunity for subsequent full partnership after approximately three additional years. Practice consists of general pediatric type practice with the exclusion of obstetrics and major surgery.

PEDIATRICIAN — Two newly associated, young pediatricians already desire third man to associate in busy and very interesting general pediatric practice. No investment necessary. Equal time off. Salary to early partnership.

INTERNISTS — Northwestern Connecticut Hospital area needs internists interested in practicing general internal medicine. Hospital area serves a 50,000 population.

GREAT OPPORTUNITY for Internists, General Practitioners, Otolaryngologist, Psychiatrists and Pediatricians in the Windham area. Solo or group practice available with hospital staff privileges. For

further information contact: Frank Bird, M.D., Windham Community Memorial Hospital, Mansfield Avenue, Willimantic 06226.

Placement Wanted

G.P.—desires emergency room position, experienced, age 50, presently in own practice.

SURGEON—38 years of age Board certified interested in a group type practice. Presently in practice. Available immediately.

INTERNIST—32 years of age, Board certified with National Boards, desires full time hospital position in cardiology, will consider partnership. Presently in practice.

OPHTHALMOLOGIST—30 years of age, Board certified with National Boards, interested in an associate type practice.

PATHOLOGIST—32 years of age, Board eligible desires associate practice in Connecticut. Presently in practice, available immediately.

PREVENTIVE MEDICINE—54 years of age, Board certified wishes to associate full-time with college age people. Presently in practice. Would like to give three months notice.

INTERNIST—47 years of age, Board eligible wishes group or associate practice in Connecticut. Military obligation completed in Turkey. Available immediately.

ORTNOPEDIST-EMERGENCY ROOM—30 years of age with National Boards interested in an institutional or industrial type practice. Military obligation completed. Available immediately.

PATHOLOGIST—40 years of age, wishes solo or group practice in Connecticut. Presently in practice with military obligation fulfilled.

UROLOGIST — 32 years of age, Board eligible wishes group or associate practice in Connecticut.

GENERAL PRACTICE—EMERGENCY ROOM—37 years of age wishes group or industrial type practice in Connecticut. Available immediately.

PEDIATRICIAN—39 years of age, wishes to practice in Connecticut. Available immediately.

ANYONE INTERESTED IN THE ABOVE IS ASKED TO CONTACT THE PHYSICIANS PLACEMENT SERVICE, 160 ST. RONAN STREET, NEW HAVEN, CONNECTICUT 06511.

In Memoriam

Burke, William F., Sarasota, Florida, Georgetown University 1928. Dr. Burke was a general practitioner in the Newtown area for many years before his retirement. He was on the staff of the Danbury Hospital. Dr. Burke was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Dr. Burke died September 14 at the age of 71.

Leonard, George A., Fort Pierce, Florida, University of Maryland 1905. Dr. Leonard was a general practitioner in the Waterbury area from 1906 until his retirement in 1940. Following his retirement from practice in Waterbury, he served as chief medical officer of the Veterans Administration Regional Office in New Orleans, La. and El Paso, Texas. Dr. Leonard was a colonel in the U.S. Army Medical Corps. He also served as a medical officer in France during World I and World War II. Dr. Leonard was a member of the American Medical Association, Connecticut State Medical Society and the New Haven County Medical Association. Dr. Leonard died October 24 at the age of 85.

Richardson, Ralph A., Bristol, University of Vermont 1914. Dr. Richardson was an internist in Bristol area until his retirement in 1955. He was the former chief of staff of the Bristol Hospital. Dr. Richardson was the first person to be honored by the Press Club of Bristol for his services to local veterans. Dr. Richardson was a member of the American Medical Association, the Connecticut State Medical Society and the Hartford County Medical Association. Dr. Richardson died October 13 at the age of 79.

Upson, William H., Suffield, Tufts University 1927. Dr. Upson was a general practitioner in the Suffield area from 1929 until he retired in 1968. He was president of the health association in 1955 and 1956 and was president of Hartford County Medical Association in 1952 and 1953. In 1942 he was appointed to the medical board of the Selective Service of Hartford County. He was assistant medical examiner of Suffield from 1949 to 1964 and was director of health for Suffield from 1951 to 1960. Dr. Upson was a member of the American Medical Association, the Connecticut State Medical Society and the Hartford County Medical Association. Dr. Upson died October 27 at the age of 68.

Medical Grand Rounds Yale-New Haven Hospital

An Unusual Case of Hyperthyroidism With A Slow Pulse

Frederick Lee Sachs, M.D. and Lewis Landsberg, M.D., Editors
Pamela A. Brooten, Assistant Editor

The patient is a 54-year-old white housewife who was admitted to Yale-New Haven Hospital for the first time on July 14, 1969, with a history of congestive heart failure of six months' duration and a recently discovered heart murmur. She was well until February, 1969, at which time she noticed increasing weakness, progressing to the point where she was unable to continue her employment as a machine operator. A twenty pound weight loss ensued. Three months before admission she developed ankle edema, dyspnea on exertion, and cough productive of small amounts of white sputum. In March she consulted a physician at which time a heart murmur was heard, and chest x-ray revealed left ventricular enlargement with clear lung fields. She was digitalized and placed on diuretics; because of the heart murmur and congestive heart failure she was referred to Yale-New Haven Hospital for evaluation.

On physical examination, she presented as a well-developed, middle-aged lady who appeared in good spirits. The blood pressure was 150/80, pulse 75 and regular, respirations 12. She was afebrile. Pertinent physical findings included the following: The conjunctivae were pale; the sclerae were not icteric. She did not have diplopia, ophthalmoplegia, or paralysis of upward gaze. Funduscopic examination was normal. The neck was supple and there was venous distention 3 cm above the clavicles at 45°. The thyroid gland was diffusely though minimally enlarged and non-tender. There were no audible bruits. Lymph nodes were unremarkable. Scattered expiratory wheezes were heard at both lung bases. The heart was enlarged with the PMI 3 cm. to the right of the mid-clavicular line. The second sound was physiologically split. There were

no heaves, shocks, or thrills. A Grade 3 out of 6 harsh, low-pitched, crescendo-decrescendo murmur was heard best in the third intercostal space along the left sternal border, radiating to the neck. Diastole was clear and gallop rhythm was absent. There were no palpable abdominal masses. There was marked pitting edema of both lower extremities including the pretibial areas. The skin was warm and dry and there was no cyanosis or clubbing. Fine tremor of the extremities was noted. There was marked weakness of the hip flexors and moderate loss of strength in the knee flexors. The patient exhibited slight wasting of the musculature about the shoulders. Deep tendon reflexes were hyperactive bilaterally. The remainder of the physical examination was unremarkable. On re-examination definite lid lag and mild exophthalmos were noted.

Laboratory data: Hematocrit 31%; red blood count 3.2 million; mean corpuscular volume 81; mean corpuscular hemoglobin; platelets 110,000; reticulocytes 0.8%; MCHC 33. Urinalysis revealed: SpG 1.014, trace protein, negative glucose, 0-1 RBC/HPF, 1-2 WBC/HPF. BUN 10 milligrams percent; FBS 130 milligrams percent; uric acid 7 milligrams percent; bicarbonate 23 milliequivalents per liter; chloride 103 milliequivalents per liter; sodium 145 milliequivalents per liter; potassium 4 milliequivalents per liter; calcium 10.1 milligrams percent; phosphate 4.3 milligrams percent; total protein 6.0 grams percent; albumin 3.4 grams percent; globulin 2.6 grams percent; gamma globulin 1.28 grams percent; beta globulin 0.87 grams percent; alpha-2 globulin 0.43 grams percent; alpha-1 globulin 0.40 grams percent; cholesterol 120 milligrams percent; free cholesterol 35 percent; fatty acids 3.2 milliequivalents per liter. Total bilirubin 1.82 milligrams percent; direct bilirubin 0.67 milligrams percent; cephalin flocculation 4+; thymol turbidity 3.3 units; alkaline phosphatase 77 units; SGOT 31 units. Direct Coombs negative; serum haptoglobulin normal; VDRL non-reactive; rheu-

DR. FREDERICK LEE SACHS, Instructor in Medicine, Yale University School of Medicine, New Haven, Connecticut.

DR. LEWIS LANDSBERG, Chief Resident, Department of Medicine, Yale University School of Medicine, New Haven, Connecticut.

matoid factor negative; antinuclear factor negative. Four blood cultures were negative. PBI 14 micrograms percent; T3 uptake 74 percent, RAI uptake at 2 hours was 60 percent, at 6 hours 77 percent, at 24 hours 72 percent. Thyroid scan revealed a diffusely enlarged gland without nodularity. EKG was unremarkable. Electromyography was consistent with myopathy.

DR. LEWIS LANDSBERG: The x-ray will be reviewed by Dr. Ronald Hoy.

DR. RONALD HOY: A cardiac series was done on July 15th. It shows a large heart with a small amount of pleural fluid bilaterally. The upper lobe vascularity is prominent. No specific chamber enlargement is demonstrable. There is no aortic valve calcification. The picture is compatible with heart failure without indicating any specific cardiac lesion.

DR. LEWIS LANDSBERG: Dr. Gerald Burrow will open the discussion.

DR. GERARD BURROW: This patient demonstrated a stare, lid lag, and a pulmonary flow murmur which I believe is due to turbulence caused by accelerated blood flow. In addition, she had an enlarged thyroid and a fine tremor of the extremities. These findings, taken with her markedly abnormal thyroid function studies, certainly confirm the diagnosis of hyperthyroidism. Although she was seen by several competent physicians before her admission to this hospital, a diagnosis of hyperthyroidism was obscured by the fact that she had concomitant heart disease. In her case, the absence of tachycardia, the lack of hyperkinetic activity, and the failure to describe heat intolerance lead one away from the correct diagnosis. It is almost as if she had been reserpinized or subjected to beta blockade before admission to the hospital. Many of the signs and symptoms attributed to an overactive thyroid which are due to sympathetic hyperactivity were not present.

This patient does not fit into the category of apathetic hyperthyroidism as described by Lahey.¹ Such patients did not have a goiter, were dull and listless, and lay quietly in bed without any predominant symptoms. They were later proved to be hyperthyroid, with a relatively serious prognosis. The patients behaved as if they were suffering from complete exhaustion.

Rather, our patient most closely resembles the category of patients termed masked hyperthyroidism. In this form concomitant disease tends to mask the symptoms of hyperthyroidism.

The four major subgroups of masked hyperthyroidism include: a) a gastrointestinal type in which the patients present with abdominal pain, or more commonly, diarrhea, and are often subjected to an extensive GI workup which is unrevealing; b) a cachectic type in which the patient enters with profound weight loss and is evaluated for possible malignancy; c) a myopathic form in which the patient presents with extreme muscle wasting; and d) a cardiac form, well illustrated by the patient presented today.

This woman obviously has Graves' disease with a diffusely enlarged thyroid and a mild degree of exophthalmos. The masked form is said to occur more commonly, however, in what Plummer called toxic nodular goiter. Graves' disease is a diffuse goiter as compared with the nodular goiter that one finds in Plummer's disease. It is thought that Graves' disease is caused by, or associated with, long-acting thyroid stimulator (LATS). If LATS is found in a patient with a nodular goiter, diffuse hyperplasia will be found surrounding the nodules; thus, one might argue that these cases merely represent Graves' disease with nodules, and pure nodular goiter is not associated with an elevated LATS. Patients with Graves' disease tend to be women in the child-bearing age. Individuals with Plummer's disease tend to be older, partly because there is a lag between the formation of the nodule and the development of autonomous function. The fact that they are older explains why the masked form of the disease are more common; older individuals are more likely to have concomitant disease aggravated by the hyperthyroidism. Bartels² states that any individual who develops multinodular goiter will become thyrotoxic provided they live long enough. In Graves' disease the laboratory data is often diagnostic. In Plummer's disease, however, the PBI may not be elevated. This may be due in part to the fact that the nodule is producing triiodothyronine which does not appear in the laboratory determination of protein-bound iodine. Therefore, one finds a normal PBI despite excessive amounts of active thyroid hormone.

Sandler and Wilson³ described a group of patients who had hyperthyroidism and heart disease. Patients were divided into those who had obvious underlying cardiac disease and those in whom the etiology of the heart disease was enigmatic. Whether it is possible to separate patients in this manner is open to question. It was concluded that although cardiac decompensation abated with the return to the euthyroid state, the hyperthyroid state, per se,

contributed to the cardiac impairment. What is perhaps more important in the discussion of Sandler and Wilson is the fact that one-third of their patients with heart disease had masked hyperthyroidism. These figures are even more striking when one considers that their definition of "overt" hyperthyroidism includes any patient in whom hyperthyroidism was even part of the differential diagnosis. Noteworthy is the fact that the patients with masked hyperthyroidism were mainly over 40 years of age, female, with small, multinodular goiters. The symptoms of diarrhea, and sweating, which we commonly associate with hyperthyroidism did not occur frequently in patients with masked hyperthyroidism and heart disease. The majority of patients with the cardiac form of masked hyperthyroidism presented with dyspnea on exertion. Four of these patients had a heart rate of less than 90. In a study of elderly patients over 65 with hyperthyroidism, Bartels² found that 54 of 91 patients had heart rates below 100 and 9 of the 54 had heart rates below 80. The reason for this finding was unclear, but it is evident that the possibility of thyrotoxicosis should be considered in any individual with goiter and heart disease.

The proper treatment of this woman is influenced by the fact that she is over the age of 40 and, therefore, could be a prime candidate for radioactive I¹³¹. In recent years it has been demonstrated that the incidence of hypothyroidism following treatment with radioactive iodine may approach 100% in some series. We have now learned that if smaller doses of radioactive iodine are given, the incidence of hypothyroidism can be greatly reduced. In a small number of individuals an exacerbation of hyperthyroidism may be noted after the administration of radioactive iodine. Thus, in an individual in whom exacerbation of the hyperthyroid state might be harmful, one must control the hyperthyroidism with drugs before administering radioactive iodine. It is impossible to do this with propylthiouracil because the dose of I¹³¹ depends on uptake of the I¹³¹ in the gland and its incorporation into thyroid hormone. If the patient is on propylthiouracil, the organification of the iodine is blocked and it is difficult to deliver an effective dose of radiation to the gland. Our usual course of action in patients with severe thyrotoxicosis is to treat with adrenergic blocking agents. These are usually used in larger doses than are normally used in the treatment of hypertension. The first agent of this type to be used was reserpine given in doses of one milligram IM every 12 hours for several days

and one milligram PO daily until the patient is brought under control. Guanethidine, in a dose of 50 milligrams a day, may also be used with subsequent doses dependent on the patient's response. More recently, propranolol, in a dose of 20 mg. three or four times a day, has been employed. It is important to remember that these sympathetic blocking agents do not affect the basic disease of hyperthyroidism. Their primary role is blocking the beta effect on the heart, so that patients do not develop congestive heart failure secondary to tachycardia and high output failure. The patient under discussion today is in a significant degree of heart failure and one should not employ beta blocking agents in her case since beta blockade also inhibits myocardial contractility. It is for this reason that I would recommend that this patient be treated with propylthiouracil. She has a gland not much enlarged and it is unlikely that she has large stores of thyroid hormone in the follicles. I think it is reasonable to expect that she will reach satisfactory control in three to four weeks.

DR. LEWIS LANDSBERG: Are there any comments?

A PHYSICIAN: Could you please elaborate on some of the laboratory tests which aid in making a diagnosis of toxic nodular goiter?

DR. GERARD BURROW: This is difficult in terms of routine laboratory tests. As I mentioned before, the PBI may not be elevated. Triiodothyronine may be determined on a research basis but is not commonly available. Probably the best way to make the diagnosis is with the use of a radioactive iodine uptake and scan. If the scan reveals nodular goiter, the patient may be placed on suppressive therapy with triiodothyronine and the I¹³¹ uptake repeated. If the nodule is autonomous, the repeat scan should show only the hyperfunctioning nodule. The use of T3 in patients with angina may be hazardous and this test should probably not be performed in patients with symptomatic coronary artery disease.

DR. LEWIS LANDSBERG: Dr. Goodyer, do you have any comments?

DR. ALAN GOODYER: The fact that this woman demonstrates bradycardia in the face of overt hyperthyroidism is an interesting one. She has demonstrated some extremely interesting physical findings. Yesterday, I attempted to determine whether she had any sympathetic innervation of her heart. Her resting pulse was 48, which is almost unheard of in hyperthyroidism. With exercise equiva-

lent to a 10-step Master's test her rate went up to 82. It is evident, therefore, that she has a sympathetic drive, as evidenced by the rise in pulse rate with exercise. Her bradycardia is unexplained and may be due to increased vagal tone. It would be interesting to see the effect of atropine on her cardiac rate.

References

1. Lahey, F. H.: Non-activated (apathetic) type of hyperthyroidism: *New Eng. J. Med.*, 204: 747, 1931.
2. Bartels, E. C.: Hyperthyroidism in patients over 65: *Geriatrics*, 20: 459, 1965.
3. Sandler, G. and Wilson, G. M.: The nature and prognosis of heart disease in thyrotoxicosis: *Quarterly J. of Med.*, 28: 347, 1959.

"Urinalysis" As Described By Hippocrates

The urine is best when the sediment is white, smooth, and consistent during the whole time, until the disease come to a crisis, for it indicates freedom from danger, and an illness of short duration; but if deficient, and if it be sometimes passed clear, and sometimes with a white and smooth sediment, the disease will be more protracted, and not so void of danger. But if the urine be reddish, and the sediment consistent and smooth, the affection, in this case, will be more protracted than the former, but still not fatal. But farinaceous sediments in the urine are bad, and still worse are the leafy; the white and thin are very bad, but the furfuraceous are still worse than these. Clouds carried about in the urine are good when white, but bad if black. When the urine is yellow and thin, it indicates that the disease is unconcocted; and if it (the disease) should be protracted, there may be danger lest the patient not hold out until the urine be concocted. But the most deadly of all kinds of urine are the fetid, watery, black, and thick; in adult men and women the black is of all kinds of urine the worst, but in children, the watery. In those who pass thin and crude urine for a length of time, if they have otherwise symptoms of convalescence, an abscess may be expected to form in the parts below the diaphragm. And fatty substances floating on the surface are to be dreaded, for they are indications of melting. And one should consider respecting the kinds of urine, which have clouds, whether they tend upwards or downwards, and the colors which they have and such as fall downwards, with the colors as described, are to be reckoned good and commended, but such as are carried upwards, with the colors as described, are to be held as bad, and are to be distrusted. But you must not allow yourself to be deceived if such urine be passed while the bladder is diseased; for then it is a symptom of the state, not of the general system, but of a particular viscus.—Runes, D. D., and Kiernan, T. (eds.): *Hippocrates: The Theory and Practice of Medicine*, New York: Philosophical Library, Inc., 1964, pp. 48-49.

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X-Ray of the Month

Section of Chest Diseases

Arnold B. Rilance, M.D.

History

A 22 year old female entered the hospital with a 7 day history of steady substernal chest pain of increasing severity. Two weeks prior to admission she developed tonsillitis following which chest pain developed with associated dysphagia. Five days prior to admission she developed an unproductive cough and noted increased pain in the chest on bending forward. An X-ray of the chest was made in the E.R. An EKG was normal. WBC-8,900. An esophogram taken the next day revealed displacement of the esophagus posteriorly and to the left by a large mediastinal mass. Apart from the symptoms noted above she had a negative past history.

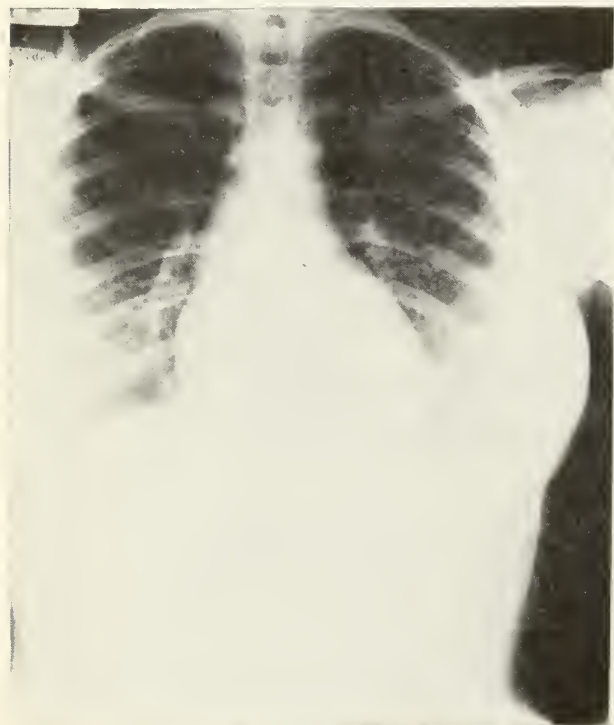


Figure 1

An X-ray (1967) taken on a prior hospital admission reveals a faintly outlined shadow just lateral to the right heart border (arrow). This was not read as abnormal.

DR. ARNOLD B. RILANCE, Director, Winchester Chest Clinics, Yale-New Haven Medical Center.

On physical examination, blood pressure was 110/75; pulse, 88. There were no enlarged peripheral glands. The lungs were clear. Examination of the heart was normal. Further studies included a G.I. series, which was normal except for esophageal displacement. A scalene node biopsy was performed with normal findings. An intermediate strength PPD was negative. A bone marrow biopsy revealed an increase in number of plasma cells and lymphocytes, no abnormal forms. Liver function tests, SGOT, LDH and alkaline phosphatase were normal.

Possible diagnoses included:

1. Lymphoma or thymoma
2. Reduplication cyst of esophagus
3. Bronchogenic cyst (mediastinal)
4. Tuberculous lymphadenopathy and sarcoidosis seemed unlikely possibilities due to the location of the mass.

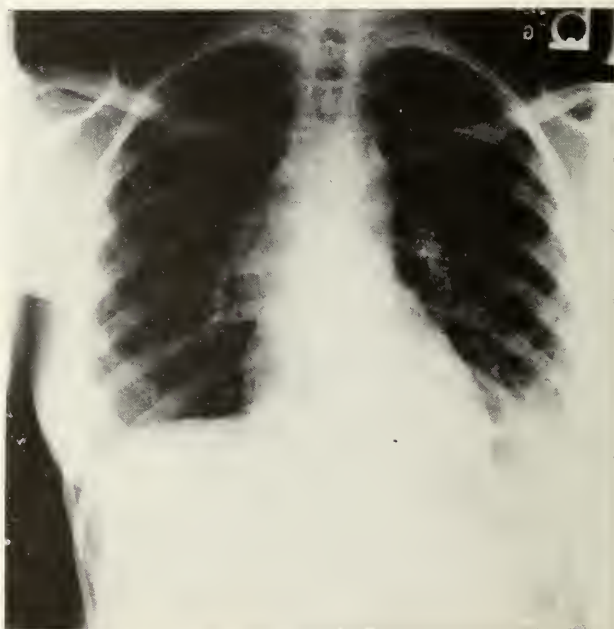


Figure 2

X-ray (6/18/69) on admission to the hospital demonstrates a sharply outlined mass lesion extending to the right of the right main bronchus. The carina markedly broadened.

An exploratory operation was performed.

A large cystic structure was removed from the mediastinum. The inner wall of the cyst was smooth with a delicate vascular network producing a pink-gray coloration.

Diagnosis

Bronchogenic cyst (mediastinal).

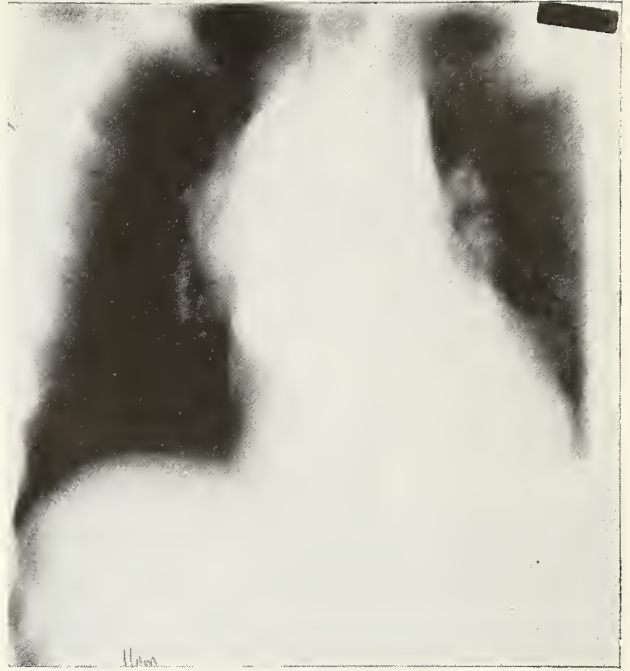


Figure 4

A.P. Laminagrams showing the widening of main carina and encroachment on the right intermediate bronchus.

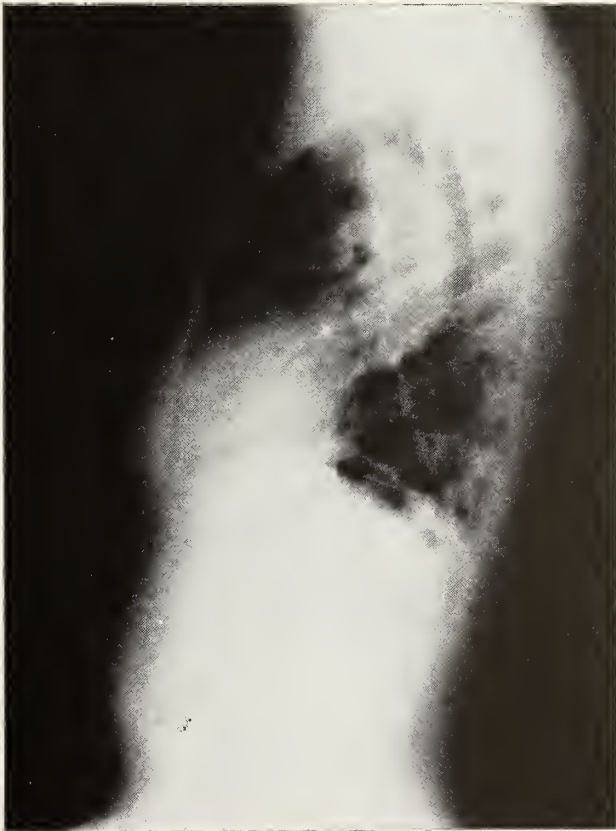


Figure 3

Lateral view shows the mass to be posteriorly and inferiorly located.

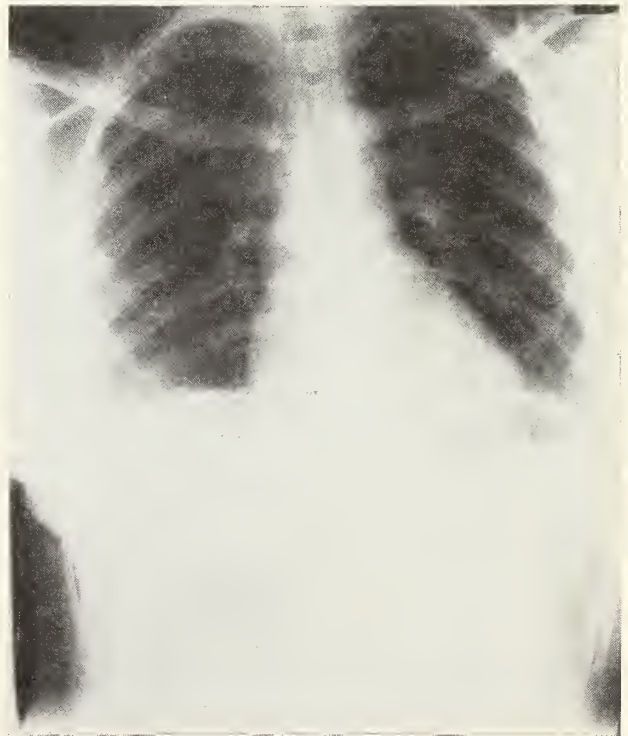


Figure 5

Post-operative film—negative.

Electrocardiogram of the Month

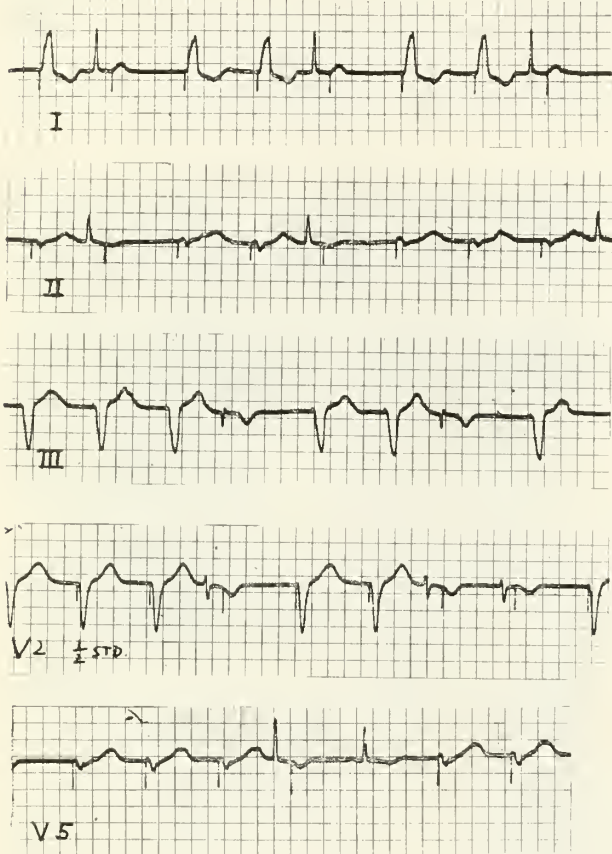
St. Mary's Hospital
Waterbury, Connecticut

Prepared by
DONALD J. WEBER, M.D.
Director of Cardiology,
St. Mary's Hospital
Fellow of the Colleges of
Physicians and Cardiology;
Council on Clinical Cardiology

The patient is a 47 year old female admitted because of episodes of fatigue and syncope. Findings were slight cardiac enlargement and sinus brady-

cardia with rates as low as 35 per minute. She was taking no drugs and had no hypertension or angina or valvular disease. Carotid pressure produced no further slowing and atropine increased the rate only ten beats per minute. Laboratory findings were unremarkable. A fixed rate pacemaker set for 70 per minute was implanted and completely controlled the cardiac mechanism with an R-P interval of .24 seconds. This cardiogram the next day showed effective pacing, but progressive delay in retrograde conduction to the atria intermittently leading to ventricular return extrasystoles at an R-P interval of .44 seconds. This is especially clear in lead II. After discharge she did well and had no further syncopal episodes.

Pacing has become an accepted procedure for severe or symptomatic bradycardia. Retrograde P waves are not unusual even in the presence of AV block but here, return extrasystoles or ventricular echoes can occur as antegrade block was not present. Presumably there is a functional longitudinal dissociation of at least part of the AV conducting system such that, following atrial depolarization, part of the conducting system or a bypass tract is capable of being stimulated and by antegrade passage can cause a ventricular systole. For return extrasystoles to occur the retrograde conduction from ventricle to atrium must be relatively prolonged thereby permitting junctional and ventricular tissue to recover from the previous depolarization.



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PRESIDENT-ELECT ATTENDS CONFERENCE

Let's tell it like it is! The accent was on youth at the 26th annual conference of state presidents, presidents-elect, National officers and chairmen of the Woman's Auxiliary to the American Medical Association, held October 5-8, 1969 at the Drake Hotel, Chicago, Ill. The conference opened with regional get-acquainted dinners where we learned a great deal from our eastern neighbors.

Dr. Gerald Dorman, President of the AMA, gave the keynote address at the opening session Monday. He stressed involving our young doctors. Arizona, for example, had just voted to make their 400 medical students members of their state society. Dr. Dorman remarked on the current lampooning of medicine in the news, TV, etc. We need better public relations to tell the MD's true story.

The public needs to know that medicine's objective is to provide the best health care for all people. Youth today is interested in involvement with people. Social work is their top interest. Posters and health career literature could be put in our husbands' offices. The Woman's Auxiliary to the Student Medical Association, WASAMA, is increasing its activity in 30 states with 70 active chapters.

Dr. Ernest Howard, executive Vice President, AMA, spoke of the serious problems confronting medicine today. They are frightening. We should all be alert to them. Senator Robert Packwood, Oregon, brought us in his address, a six point plan, "You, Too, Can Be A Leader." For those auxiliary members with an interest in politics they are: purpose, integrity (believe in your party), tolerance (you might be wrong), discipline, change (learn from history, there is no "best" way, only "better"), and last, imagination.

As you can deduct this conference had a great program. The speakers were top-notch, the programs well planned and on time! The friendliness

of all was outstanding. It was exciting to meet with women from all of our 50 states informally and to exchange ideas: If our state auxiliary members could only capture the excitement, we would do away with the ever present question—"What does the auxiliary do?"

What programs did we bring back to get busy on? This year the stress is on the following:

Highway Safety—We can talk to our state legislators and show concern, help implement defensive driving courses, join the Woman's National Safety Council.

Drug Abuse—We can educate parents and teacher (teens are often well-informed), enlist police aid in presenting programs.

Alcohol and Its Dangers—Excellent new film-strip available, "A New Look at the Old Sauce".

Community Health—Focus on: blood donor programs, violence on television, hearing and visual screening programs, immunization, placing Today's Health Guide in schools and libraries, sex education.

International Health — Many instructions are available for making sleeping mats, quilts, exercise balls, leper bandages. Involve your church groups in making these items. Invite foreign wives to meetings, entertain them. Send MD's Wife to foreign wives.

Medicine and Religion—There is a new half-hour film "A Storm, A Strife" on this subject. Hope we can bring it to Connecticut next year.

And, most important, we have AMA-ERF and Health Careers to work on and many more jobs than we have workers. Here in Connecticut we are just beginning the job. With all this to be done, don't you have a special interest? Let us know what you are doing in your town.

Mrs. John Mendillo, *President-elect*

AROUND THE STATE

New Haven County 186th Semi-Annual Meeting New Haven County Medical Association October 23, 1969

The 186th semi-annual meeting of the New Haven Medical Association took place at the Waverly Inn on October 23, 1969.

President Pelz called for a standing moment of silence in memory of our seven deceased members in 1969. They were: Drs. Alexander Bassin, Charles Lee Buxton, John J. Casagrande, Edward H. Kirschbaum, William M. O'Connell, Wilder Tileston and James S. VanLeuvan.

Thirty-three new members were elected to provisional membership. They were: Peter Chodoff, New Haven; Robert V. P. Hutter, New Haven; Richard H. Mattson, New Haven; John V. Price, Waterbury; Frederick P. Anderson, New Haven; Sandra P. Boltax, New Haven; Peter G. Burch, Meriden; Wilfredo E. Cadelina, Derby; John M. Christoforo, New Haven; Nicholas A. Coassin, Milford; Alan Cahn Davidson, Derby; Julio E. DeMarchena, Middlebury; David Michael Dressler, New Haven; Andrew John Fezza, Hamden; James J. Fischer, New Haven; Gerald Stanley Freedman, New Haven; Arthur I. Geltzer, New Haven; Francis James Kenney, Waterbury; Robert Anthony Lanzi, Orange; Ira Richard Levine, West Haven; Michael Richard Longo, Jr., Meriden; Stanley Eugene Matyszewski, Waterbury; Melvin R. Ostrov, Waterbury; Ludwig J. Pavlo, Ansonia; Maria M. Pavlo, Ansonia; Eric Anthony Sailer, New Haven; Solomon S. Schwartz, New Haven; Gilbert B. Solitare, New Haven; Charles Joep VanDerHeide, New Haven; Harvey Allen Weitzman, West Haven; Lloyd Mather Wilcox, New Haven; Emanuel Claud Wolff, West Haven; Hee R. Yoon, Milford.

Among the honored guests representing the Connecticut State Medical Society were: Dr. Stevens Martin, President; Dr. Morris Granoff, President-elect; Dr. William R. Richards, Executive Director; Dr. Kenneth Brandon, Speaker of the House of Delegates; Dr. Frank Abbot, Vice-speaker of the House of Delegates and Dr. Charles Polivy, Councilor at large. Also Dr. Leo Giardi, President of the Connecticut State Academy of General Practice and Dr. T. F. Nolan, the Delegate from the Fairfield County Medical Association.

Six of New Haven County's seven delegates to the other counties attended the various other county semi-annual meetings this fall and reported on their experiences. This full attendance effort by New Haven County delegates may well represent something of a record in the annals of the county delegate system in the State of Connecticut and probably should be cited.

Our Councilor, Dr. Stewart Petrie, reported on CRMP, Medicaid and COMPAC in addition to the subject matter of his previously printed councilor's report.

The New Haven County Medical Association voted to increase the scope of its activities and to hire additional office help. This determination resulted in the approval by the association of an increase in annual dues of \$15.00.

The New Haven County Medical Association voted overwhelmingly to retain its present rule on Compulsory Attendance which is similar to the rules now in effect in Fairfield and Hartford Counties.

The New Haven County Medical Association voted at the semi-annual meeting to support COMPAC and to urge the provision of specific funds for COMPAC educational activities by the Connecticut State Medical Society.

The annual meeting of the New Haven County Medical Association will take place on Thursday, March 19, 1970 at the Waverly Inn, and the semi-annual meeting will take place on Thursday, October 22, 1970 at the Waverly Inn.

The semi-annual meeting of the Connecticut State Medical Society's House of Delegates will take place on December 11, 1969 at the New Haven Medical Association Building, 362 Whitney Avenue, New Haven.

At the subsequent dinner meeting at which Dr. Stewart Petrie acted as master of ceremonies in conducting the drawings for the multitude of valuable door prizes, an award was presented to Dr. Hyman A. Levin, Clerk of New Haven County for the previous ten years. The award read: "In grateful recognition for a lifetime of dedicated service".

Respectfully submitted,

WILLIAM L. WEST, M.D., Clerk

Freezing Controls Oral Cancer Resistant To Standard Therapy

(*JAMA*, 208: 456, April 21, 1969) A dozen patients who had persistent oral cancer after standard approaches were treated by cryosurgery and it seemed an effective means of controlling the squamous cell cancers. The patients were treated by Dr. Jerrie Cherry on an outpatient basis twice a week until the tumor sloughed off.

No recurrence of carcinoma has occurred in the patients during follow-up ranging from 6-14 months. A standard cryoprobe for oral lesions was used. Some patients received local anesthesia, others underwent cryosurgery without anesthesia.

During each treatment session the tumor tissue was frozen for three minutes, allowed to thaw then frozen again for three minutes. Tissue temperature at the time of freezing was around -17° . In all cases the tumor tissue eventually died and sloughed off.

It appears that cryosurgery is a safe, painless technique and effective. There remains more work to be done with the cryoprobe before its usefulness can be accurately evaluated.—L.H.N.

New Concepts In University Community Mental Health Services

(*JAMA*, 208: 2453, June 30, 1969) A pilot project designed to help meet mental health needs of the student population of the University of Pennsylvania is described. It consists of a group of medical students under faculty supervision that offer advisory service to assist troubled college students who are reluctant to seek formal psychiatric care because of fears of its "stigma," suspicion of university administration and/or a belief that older professional personnel cannot understand the problems of their generation.

A medical student advisor has unique positive attributes of clinical training and experience yet is of peer age. Walk-in centers (talking points) located at strategic areas on campus are manned during key hours. Complete anonymity is guaranteed. Then Psychiatric staff members hold regular supervisory sessions to review cases.

In the first 14 weeks of operation 71 clients were seen. Problems have included depression, social maladjustment, incipient psychosis, fear of pregnancy and suicidal attempts. Those requiring professional care are then referred.—L.H.N.

Draft Caused Drop In Graduate Science Enrollment

(*Science*, 165: 162, July 11, 1969) The draft caused a pronounced drop in graduate science enrollments in the fall of 1968 and then caused still further attrition during the school year. The National Academy of Sciences warned that existing draft rules "alarmingly" reduce the flow of individuals into scientific and technical areas.

Responses from 304 of 508 departments surveyed indicate that 15.4 per cent of first-year male students and 11.8 per cent of second-year men either entered service or been ordered for induction prior to June 1969. Chemistry was hit harder than physics or psychology. One small department lost 71 per cent of its first and second-year students while other departments lost only 3-4 per cent.

Many department heads also noted that they had suffered "severe" losses of graduate students even before the 1968 fall term began, so the losses covered by the survey were in a sense "additional" losses. The outlook for the next academic year barring a change in the draft laws or the war—is bleak in the eyes of respondents to the survey.

Two university chemistry departments reported that graduate acceptances for next fall are down by more than half from the previous year. One chemistry department that is co-educational said its entire incoming class for 1969 will consist of females only.

Even then the survey did not measure the full loss of graduate students brought about by the draft, since it did not count those students who dropped out of school to seek jobs that might qualify for occupational deferment, those who changed from full time student status to full time teaching status in hope of gaining occupational deferment, those whose local boards had promised induction notices during the summer and those who had accepted graduate appointments for next fall but then withdrew because of the draft.—L.H.N.

The Coronary Care Unit: A Time For Reflection

(*JAMA*, 209: 22, July 7, 1969) The Second National Conference on Coronary Care Unit (CCU) met in Denver recently and reviewed the benefits of these units in the last two years. The Conferees believed the units had saved many lives and at the same time had brought about a new partnership of physician and nurse which is important for care of the coronary patient of the future.

The CCU in the U.S. have grown from 400 two years ago to 1,500 today. However, an estimated 6,000 four bed units would be needed to provide coverage for the population at large. Despite the success of units so far there remain need for training more nurses and physicians particularly a physician to act as unit director, decision maker, and guiding hand. This is needed to prevent a situation where a nurse is more knowledgeable in CCU operation than some attending physicians.

Physician training programs are operating around the nation, several of which were described to the delegates. Uniting the physician and nurse in "team approach" was advocated. Other recommendations were to improve evaluation techniques of the training of CCU personnel and actual or simulated situations should be used to check performance. Better records on CC patients and their response to drugs were needed. Focus more attention on sudden coronary deaths and mobile CCU units should be carefully studied for performance.

Some delegates thought that delay in seeking treatment is a major factor in coronary deaths. They advocated education programs, emphasizing early detection and prompt treatment, both for the physician and the public. One study showed that "victim with acute symptoms waited an average of three hours before seeking medical help." More than half of the patients had intermittent chest pains within a week prior to primary acute symptoms. This does not include the almost 50 per cent of cases of sudden death that never reach a hospital.—L.H.N.

Statewide Study of Chloramphenicol Therapy And Fatal Aplastic Anemia

(R. O. Wallerstein et al, *JAMA*, 208: 2045, June 16, 1969) Fatal aplastic anemia is a rare disorder occurring in 2 per million population each year. Death usually follows overwhelming infection or hemorrhage or both. The course of onset of anemia to death is often only a few months.

Fatal aplastic anemia appeared to be 13 times more frequent after the use of chloramphenicol. Anemia may not appear until the second or even third course of chloramphenicol therapy and it is not related to dosage.—L.H.N.

Neurochemistry At Strassbourg

(*Scientific Research*, 4: 22, March 29, 1969) Dr. Paul Mandel, the director of the Centre de Neurochimie in Strassbourg, France is concentrating the research in areas where a chemical approach to important disorders of the nervous system seems more likely to bear fruit. Among important current work is a study of aggression in rats, epilepsy in mutations in mice, biochemical mechanisms of sleep, neurochemical reactions in the retina, metabolism of nucleic acids in the nervous system membranes, including biosynthesis of membranes and changes in their metabolism.

They found a high rate of RNA synthesis in mammalian brain. Looking for an explanation, Mandel speculates, that cell neurons are secreting cells. In contrast to the usual endocrine or glandular secretion the protein secreted in neurons follow the axon flow to the nerve endings and may even enter the effector cell.

They are also interested in the correlations between protein intake and alertness. Using rats they have demonstrated that a chronic decrease of tyrosine and tryptophan intake in diet produces an increase of about 50 per cent in sleep during the day. This undernutrition may explain the lower alertness sometimes observed in developing countries.—L.H.N.

Herpes Globulin Prevents Varicella

(*JAMA*, 208: 2001, June 16, 1969) Dr. Philip A. Brunell prepared immune globulin from plasma of donors recovering from herpes zoster infection since herpes zoster and varicella are caused by the same virus. He then gave it to children exposed to varicella within 72 hours after exposure. None of the children who received the immune globulin contracted varicella. The dosage required was 0.05 to 0.07 ml. per pound of body weight. The minimum amount may be less and studies are underway to determine this as well as the adult dose.—L.H.N.

MEETINGS

GENERAL

May 12, 13, 14

178th Annual Meeting

Connecticut State Medical Society

Hartford-Hilton Hotel, Hartford

MEDICINE

Weekly Oncology Courses

12 Noon

Hospital of St. Raphael, Radiation Therapy

Conference Room

Thursday, December 18, Antimetabolites

Joseph R. Bertino, M.D.

No meeting Christmas Day and New Year's Day.

January 9

8:30 A.M.-5:30 P.M.

Peter Bent Brigham Postgraduate Medical Series

Boston, Mass.

Coronary Artery Disease, Diagnosis and

Management

Richard Gorlin, M.D., Chief,

Cardiovascular Division

SURGERY

January 15

Annual Meeting, Connecticut Chapter,

American College of Surgeons

Park Plaza Hotel, New Haven

Panel on Surgical Education and Training, begin-

ning at 3:30 P.M., followed by a business meeting;

social hour and dinner in the evening.

Contact Francis M. Hall, M.D., 140 Woodland

Street, Hartford

March 7

11th Annual Postgraduate Anesthesia Seminar

New Jersey State Society of Anesthesiologists

Cherry Hill Inn, Cherry Hill, N.J.

Registration fee (including luncheon) \$14.00 to non-

members; interns and anesthesiology residents ad-

mitted free

May 6, 7, 8

43rd Annual New York Eye and Ear Infirmary

Clinical Conference

Biltmore Hotel, New York City

Held in conjunction with the 150th Anniversary

celebration of the New York Eye and Ear Infir-

mary. An open house will be held at the New

York Eye and Ear Infirmary on Saturday, May 9,

featuring scientific exhibits and demonstrations

of newer instrumentation and techniques.

Contact Jane Stark, Executive Secretary, 310 East

14th Street, New York, N.Y. 10003.

The Water Factor

(Schroeder, H. A.: *New England Journal of Medicine*, 280: 836, April 10, 1969.) Statistical treatment of data revealed an inverse relation between hardness of municipal water by states and death rates from the secondary effects of hypertension and atherosclerosis. Something that is not calcium or magnesium influences the deaths. If it is not calcium or magnesium what is it? Schroeder thinks it is cadmium and speculates as to how it does this. Soft water dissolves cadmium from zinc in galvanized pipes and also dissolves copper from copper pipes and a large amount of cadmium exceeding allowable limits of 10 mg. per liter by two to eight times at the tap.

Schroeder quotes Anderson le Riche and Mackay who advanced an intriguing hypothesis that the water factor may be the result of an increased tendency to sudden and lethal arrhythmias after coronary occlusion in residents in soft water areas.

If the patients also developed hypertension, then it enhances atherosclerosis, promotes cerebral hemorrhage and could easily make an acutely damaged myocardium susceptible to arrhythmias. The mystery remains unsolved and the factor in soft water that promotes hypertension, atherosclerosis and sudden death needs further study.—L.H.N.

M.D.'s Assess Abortion Law

(*JAMA*, 208: 2006, June 16, 1969) Maryland is one of six states which have adopted an American Law Institute recommendation permitting therapeutic abortion when the fetus appears to have congenital deformities. Others are Arkansas, Colorado, Georgia, New Mexico and North Carolina.

The old Maryland law allowed a pregnancy to be terminated only if a panel of physicians ruled the birth would endanger the mother's life. A new ground for abortion under the 1968 law is "a threat to the mother's mental health."

Of 651 cases, reasons given by physicians for terminating pregnancies included mental well-being of mother, 613; mother's physical well-being, 17; rape, 9; and congenital deformity, 12.—L.H.N.

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NEW BOOKS IN REVIEW

A SYNOPSIS OF CONTEMPORARY PSYCHIATRY, 4th Edition. Edited by George A. Ulett, M.D. and D. Wells Goodrich, M.D. The C. V. Mosby Company, St. Louis, 1969. 340 pp. \$9.50.

Reviewed by: LOUIS H. NAHUM

The last edition of this excellent synopsis was in 1965. The boundaries of psychiatry since then have expanded from microbiology and genetics to prenatal and post-natal influences upon intelligence, learning, conditioning and much else. Related subjects such as law, sociology and politics now need to understand psychiatry more than ever. There are a host of new workers with various levels of training in hundreds of new community mental health centers, social work schools who need a synopsis of psychiatry.

This is a concise eclectic compilation to serve as an introduction to the complex field for the beginning medical student, social worker, nurse, and mental health worker. It is a comprehensive topic review for the already initiated and a concise pocket compendium for the busy physician. It can be used as a quick reference for psychiatric residents and psychological interns especially during the initial period of specialty training and until he has had sufficient time to become acquainted with more extensive treatises.

It is written also for the general physician who is having his attention increasingly directed to the psychological problems of his patients and who most often provide each case for those of his patients who develop mental illness. Theory is kept to a minimum. It is organized into three general areas, history taking and diagnostic procedures; clinical syndromes and finally therapeutic measures. There are a few references after each chapter and also an alphabeticized general index at the back of the book. This book will fill a real need and should be of inestimable help to those who must understand, in brief, contemporary psychiatry.

A CONTROLLED CLINICAL TRIAL OF A DIET HIGH IN UNSATURATED FAT. American Heart Association Monograph No. 25. Edited by Seymour Dayton, M.D. et al. American Heart Association, Inc., New York, 1969. 63 pp. \$4.00.

Reviewed by: LOUIS H. NAHUM

Middle-aged and elderly male veterans living in Los Angeles domicile were asked to volunteer for the study. There was a control group living on a diet of 40 per cent fat calories. The experimental diet substituted unsaturated for saturated fat and was made palatable, it was also moderately low in cholesterol.

The experimental diet induced a prompt drop in serum cholesterol levels amounting to 12.7 per cent. Other results were in control and experimental groups: (1) definite silent myocardial infarction 4 and 9, definite overt myocardial infarction 40 and 27, sudden death due to coronary heart disease 27 and 18, definite cerebral infarction 22 and 13. Fatal atherosclerotic events numbered 70 in the control group and 48 in experimental group. For all primary and end secondary end points combined, 8 year incidence rates were 47.7 and 31.3 per cent.

Most of the prophylactic effect occurred in the younger half of the study population less than 65.5 years old at the start of the study.

Grading of the extent of atheromata in individuals who died and were autopsied failed to reveal significant differences between the control groups and experimental groups. The same was true of arterial total lipid and calcium concentration. Relative abundance of major lipid fractions in coronary atheromata and circle of Willis appeared independent of diet.

Thus the data do not suffice for any confident conclusions as to relative effects of the experimental diet upon different end points, but magnitude of the effect on cerebral infarction seemed impressive. At a given age cerebral atherosclerosis is less advanced than coronary atherosclerosis and this suggests that in elderly men cerebral complications are more preventable.

It would be desirable to know how much "lag time" exists before the clinical effects of serum cholesterol lowering are fully manifest. It does, however, appear that for "hard" end points there was no difference in the first year but that a great deal of the ultimate divergence of the incidence curves occurred in the second and third years.

SYMPOSIUM ON RENAL TRANSPLANTATION. Archives of Internal Medicine Symposia, Vol. 2. Guest Editor: Roscoe R. Robinson, M.D. American Medical Association, 1969. 567 pp. \$1.00.

Reviewed by: BERNARD LYTTON

There seems to be little doubt that renal transplantation has become established as an acceptable therapeutic modality for the treatment of chronic renal failure. It is applicable to about 20 percent of the 35,000 persons who die from this cause each year in the United States. A careful and well-presented analysis of the data on 512 uremic patients seen at Duke University Medical Center is contained in the contribution by Drs. Hayes and Gunnells to the Symposium on Renal Transplantation, and provides detailed support for the aforementioned statistics submitted by the Gottschalk Committee on Chronic Renal Disease to the Bureau of the Budget. It is apparent from their review, moreover, that a suitable live donor would be available in less than 25 percent of cases eligible for renal transplantation, thus emphasizing the importance of developing the transplantation of cadaver kidneys.

It has been suggested and publicized by some surgeons with wide experience in organ transplantation that kidney transplantation has already advanced to the stage where it can be performed as a community hospital service. A review of the ten contributions to the Symposium on Renal Transplantation with its authors from the diverse specialties of surgery, immunology, internal medicine, and metabolism should tend to contradict this notion. It serves to emphasize that while the results of transplantation, described by Dr. Marchioro, have improved, many major and complex problems remain to be solved. It is apparent that organ transplantation should remain at the present time in the province of the major medical centers where the talents of many experts in the various

relevant specialities can continue to be used to answer many of the outstanding questions and lead to further progress in the field.

Dr. Marchioro's account of the results are based primarily on the reports of the Kidney Transplant Registry which collates data from 89 centers in the United States and abroad. He has amplified these with the results from several institutions which have had many years experience and which have made significant contributions to the problem. It is apparent from these that the transplantation of cadaver kidneys is indeed becoming more successful. Transplantation in children is becoming more acceptable and second transplants are fairly successful provided there is an adequate interval of at least two months between the placement of the grafts.

Kidney transplantation has also provided an opportunity for research into related problems such as the pathogenesis of glomerulonephritis, and this is well-summarized in the article by Dr. Dixon and his colleagues who have contributed a great deal to the understanding of the immunological processes involved in the pathogenesis of various forms of nephritis. The role of the kidney in calcium homeostasis has been further elucidated by Bricker and his co-authors in their observations on the effects of the transplanted kidney on induced hyperparathyroidism occurring in cases of chronic renal insufficiency. The paper on The Control of Allograft Rejection by Drs. Carpenter and Merrill provides an excellent review of the current status of this problem and an evaluation of the available immunosuppressive agents. Dr. Ginn's report on the late medical complications of transplantation emphasizes, however, the continuing problems associated with immunosuppressive treatment particularly those related to the very high doses of steroids which are used. There is a brief account of the preoperative assessment of histocompatibility, but it is a pity that the authors did not take the opportunity to give a simple outline of the immunogenetic basis underlying this type of examination.

The ten contributions of the Symposium on Renal Transplantation ably edited by Dr. Roscoe R. Robinson, who summarizes the aims of the Symposium in his introduction, provide an excellent synopsis of the current status and problems of renal transplantation for any interested practitioners or students. Each paper is accompanied by an extensive bibliography so that anyone who wishes to obtain more detailed information on many of the aspects of kidney transplantation can easily be directed to the relevant literature.

GENETICS AND COUNSELING IN MEDICAL PRACTICE. Edited by Leonard E. Reisman, M.D. and Adam P. Matheny, Jr., Ph.D. The C. V. Mosby Company, St. Louis, 1969. 215 pp. with 86 illustrations. \$12.75.

Reviewed by: MARGRETTA SEASHORE

The chapters in this book discuss probabilities in genetic counselling, birth defects, chromosomal abnormalities, inborn metabolic errors, twins, cancer, and mental retardation. References at the end of each chapter and a list of general references at the end of the book lead the interested reader to further sources.

The book is not intended as an exhaustive treatise on human genetics but is written as a simplified, practical guidebook to the problems of inherited disease. The authors present concisely facts about common genetic problems in diagnosis, counselling, and interpretation of genetic consultation.

The book fulfills many of its goals. Its scope is broad, but emphasis is placed on the more common genetic disorders. The chapter on probability and statistics is careful to point out the pitfalls of actuarial risk figures. It emphasizes the importance of putting risks in context for families and individual patients. The chapter on Down's Syndrome is appropriately long and clear with helpful risk and incidence figures for this most common chromosomal abnormality. There are clear concepts in counselling in the section on antihemophilic globulin deficiency. As is illustrated by phenylketonuria in the chapter on the inborn errors, emphasis is placed on diagnosis of the affliction and its genetic implications not on therapy. There are many good photographs and karyotypes illustrating diseases which present with peculiar physical findings and clarifying points about chromosomal analysis.

There are inherent weaknesses in a book presenting a simplistic view in the interest of brevity. It fails to evaluate critically certain statements which lead to ambiguities. A few errors have crept in. The paragraph about testicular feminization is erroneous. Recent evidence indicates normal production of androgen to which end organs fail to respond, rather than testicular estrogen secretion as the authors suggest. The chapter on sex chromosome abnormalities is ambiguous and suggests initially that these difficulties should present few counselling problems. Later the authors seem to refute themselves and properly stress the importance of psychologic issues. The implication that realistic child bearing potential be early inculcated in the child flies in the face of pediatric developmental principles. On page 95, the captions for two karyotypes are reversed, and the pictures of affected children accompany the wrong karyotype. The enzyme involved in homocystinuria is cystathionine synthase not "synthetase", and homocystine, not "homocystinuria" is found in plasma and urine. The Fanconi Syndrome may be caused by diseases other than cystinosis. Furthermore, penicillamine is not therapeutically useful in cystinosis. Contrary to the chart, female carriers of nephrogenic diabetes insipidus have been detected.

Aside from the errors mentioned, the book fulfills its purpose. It would be a valuable addition to the library of the practicing pediatrician, obstetrician, and family physician.

Long-Term Anticoagulant Prophylaxis After Myocardial Infarction

(Seman, A. H. et al: New England J. Med., 281: 115, July 17, 1969.) In a double blind randomized test long-term prophylactic anticoagulant therapy after acute myocardial infarction did not reduce mortality rate or complications. More treated patients required hospitalization than patients not receiving anticoagulant drugs. Patients continually entered the study between 1956 and 1967. The average period at risk was about six years. All patients received six weeks of anticoagulant therapy for initial episodes of infarction and time and circumstances permitting for recurrent myocardial infarction.—L.H.N.



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First Rubella Vaccine OK'd

(*JAMA*, 208: 2004, June 16, 1969) A live attenuated rubella vaccine grown on duck embryo culture has been licensed by the Division of Biologic Standards of the National Institutes of Health. The first licensee Merck & Company says 600,000 doses have been produced and 2 million will be available by August 1. Eight million children could be immunized this year. As of June Congress had not appropriated funds requested for the project.—L.H.N.

Current Problems In Health Care

(Cohen, Wilbur J.: *New England J. Med.*, 281: 193, July 24, 1969.) The American health care is not really a "system" but is essentially a mosaic of public and private health programs. It grew piecemeal to meet needs as they arose. They have certain advantages but also face serious problems.

Some such as shortages of personnel are not easily corrected, but serious deficiencies in the organization and financing of health care in the United States can be effectively improved. In particular health insurance both public and private must be expanded to provide comprehensive protection for all and to cover ambulatory as well as hospital services.

Special efforts must also be made to contain costs, to reduce excessive use of hospitals, to stimulate economic operation, and to eliminate duplication by proper incentive programs to remove impediments to group practice, and to expand the numbers engaged in health care.—L.H.N.

Pacer May Work For Decade

(*JAMA*, 208: 2265, June 23, 1969.) The world's first known nuclear powered cardiac pacemaker expected to function at least 10 years and possibly 20 has been successfully implanted in a dog at the National Heart Institute, Bethesda, Maryland.

The power source is plutonium 238 chosen because it emits high energy particles with very low penetrating power. It weighs 3-1/2 ounces is 1-3/16 inches wide, 1-7/8 inches deep and 7-7/16 inches long.

The present pacemakers are powered by mercury cells and have a limited life-time due to battery depletion. The radiation emitted to tissue immediately surrounding the nuclear pacemaker is less than 5 millirads/hour and 1/2 cm. away tissues receive less than 0.3 millirads of power.

The cost will be probably 2-3 times more expensive than a regular pacemaker.—L.H.N.

A Controlled Trial Of Dexamethasone Snuff In Chronic Perennial Rhinitis

(*Lancet*, I: 968, May 10, 1969.) These workers did a double-blind study of corticosteroid snuff treatment carried out in a hundred patients with severe chronic perennial rhinitis of at least three years duration. Symptomatic improvement was greater in patients who took dexamethasone snuff 0.5 mg. daily than in those who used hydrocortisone snuff 15 mg. daily or a placebo capsule.

Dexamethasone snuff seemed to be equally successful in individuals with allergic and non allergic rhinitis and in a twelve month follow-up period prolonged good results were noted with smaller occasional doses of treatment.

The treatment is probably mainly local in effect and corticotrophin-stimulation tests suggested that suprarenal suppression was unlikely to be a frequent complication.

The patients needed to be carefully instructed in the use of the treatment. First a nasal decongestant drop was used to clear the passages if the nose was blocked. Antihistamines were taken orally if there was rhinorrhea. The powder from a pierced capsule was put into both nostrils with a special insufflator in four doses during the day using approximately one-quarter of a capsule with each insufflation. The powder was not sniffed up the nose because this tended to carry it through the nose into the pharynx.—L.H.N.

When The Best Treatment Is None

(*JAMA*, 208: 2423, June 30, 1969) Dr. Richard Goldbloom told the Canadian Medical Association that a child victim of both emotional and physical deprivation can simulate celiac disease but needs no treatment except good meals and an understanding environment. Other conditions also not needing treatment are popliteal cysts which regress spontaneously if left alone. Other conditions that worry parents but need no treatment are hemangiomas except when located over cartilage, geographic or peeling tongue, harlequin coloring in low birth weight, babies so-called pseudo strabismus and knock knee.

He warned against using antibiotics in salmonellosis unless the clinical illness is extremely severe.

If treated with antibiotics the child may continue to excrete organisms for 24-50 weeks. Untreated the organisms disappear in about 12 weeks.—L.H.N.

Hunger Clears Way For Infection

(*JAMA*, 209: 502, July 28, 1960) Dr. Nevin S. Scrimshaw described effects of hunger as cumulative. Infection worsens nutritional status by reducing food intake interfering with the absorption of nutrients and increasing their metabolic loss, and malnutrition in turn worsens the consequences of infection by interfering with normal resistance mechanisms.

Investigation of deaths in four highland Mayan Indian villages in Guatemala over a two year period indicated that two-fifths were associated with clinical signs of severe Kwashiorkor but always with a preceding episode of an acute infection that precipitated severe protein deficiency in children of borderline nutritional status. Most of the remainder were deaths associated with common communicable diseases of childhood or diarrhea.

Three villages averaging 1,000 population had poor environmental sanitation, little medical care, high mortality and morbidity plus widespread malnutrition especially among preschool children. The village that was well fed experimentally had some decrease in disease incidence and the children grew larger and better.

In the "medical care" village deaths were fewer among infants and preschool children. As a result of the study, Dr. Scrimshaw believes reduction of high morbidity and mortality in the children can come only from a "public health approach based on concerted action against multiple factors, social as well as biological—responsible for malnutrition and infection."—L.H.N.

The Electrocardiometer 15-Second Test Checks Heart Health

(*JAMA*, 209: 449, July 28, 1969) A new instrument electrocardiometer devised by Dr. D. K. Bloomfield and Harry Zuske can determine in 95 per cent of cases whether a person's electrocardiogram is normal or whether he needs a cardiological examination including a 12 lead electrocardiogram.

The subjects sit in a chair and dip their fingers into cups of saline solution. In 15 seconds a needle swings on a nearby dial—to the right if the reading is normal; to the left if a full lead ECG is indicated.

If the reading is normal the chances of having a normal 12 lead electrocardiogram are better than 95 per cent. If there is an abnormal L I then the patient needs a cardiological examination and a 12 lead ECG.

The electrocardiometer measures the height of the R wave and T wave in relation to a base line and determines whether the T wave is more or less than 14 per cent of the R wave. Two per cent of normal tracings will have a T wave of less than 14 per cent of the R wave. On the other hand 80 per cent of an unselected group of abnormal tracings will have a T wave that is either inverted or less than 14 per cent of the R wave.

A single technician could screen 8,000 persons in a single week with the new unit. If all adults over 35 were screened, 25 per cent would show some abnormalities Dr. Bloomfield estimates.

Besides mass screening there are other potential uses for the instrument. For example airline pilots who soon will be responsible for 400-500 lives in the new jumbo jets could take a quick hand dip before each flight to determine if there had been any change in their ECG's.—L.H.N.

Human Liposarcomas: Tissue Cultures Containing Foci Of Transplated Cells With Viral Particles

(Morton, D. L., Hall, W. T. and Malmgren, R. A.: *Science*, 165: 813, August 22, 1969) There is no direct evidence for the role of viruses in the etiology of human neoplasia. However, immunologic evidence suggests the association of an infectious agent with human osteosarcomas. Antibodies to osteosarcomas were demonstrated by immunofluorescence in the serums of patients with this disease and their close associates. Also hamsters develop a low incidence of osteosarcomas after inoculation with extracts of human osteosarcomas.

The authors now describe viral particles occurring foci of human liposarcoma cells in tissue culture which are morphologically similar to the sarcoma viruses of avian and murine species. Anti-bodies in the serum of the patient from whom the culture was originated reacted with cytoplasmic antigens in the original liposarcoma and in the cultured liposarcoma cells.

The observed virus particles were not due to contamination by known avian or murine viruses and cell-lines because there were no such studies in their laboratory and the liposarcoma cell line has a human karyotype.—L.H.N.

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